Neutron radiobiology: where we are

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[4] Instituto de Investigación Biosanitaria (ibs.GRANADA)

why neutron radiobiology?

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we have

- neutrons
- cells

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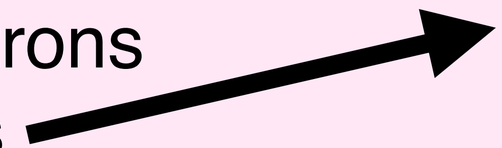

human cells of living humans

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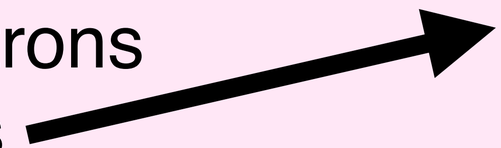

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- high-energy X-rays, electrons,
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- 20 million new cases in 2022
- 10.3 million men (lung-15.3% / prostate-14.2% / colorectal-10.4%)
- 9.7 million women (breast-23.8% / lung-9.4% / colorectal-8.9%)

leading cause of death worldwide

> 9.7 million deaths in 2022

more than half of cancer patients undergo radiotherapy

World Health Organization

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biological effects depend on: absorbed dose rate, but also on treatment fractionation, radiation quality, cell characteristics, cell environment, end points, …

absorbed dose  biological effects

absorbed dose ⟷ biological effects

weighting factors

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relative biological effectiveness (RBE)

ratio between absorbed doses delivered with two radiation qualities that result in the same effect in a given biological system, under identical conditions

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one of them a reference, usually ^{60}Co

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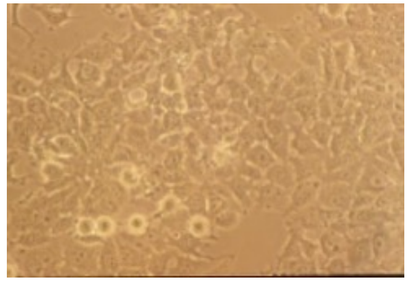
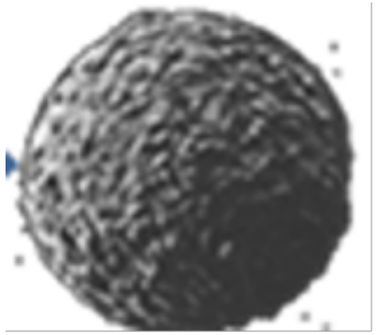
not only cell type or radiation quality





importance of the end points

- cell survival (monolayer / spheroids / matrigel)
- chromosomal aberrations
- molecular damage to DNA (simple- / double-strand breaks)
- other molecular end-points (tumor microenvironment / metastases)

RBE of neutrons

for a given radiation quality, depends markedly with

- **dose**
- **biological system**
- **effect**

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IAEA, TRS-461, 2008

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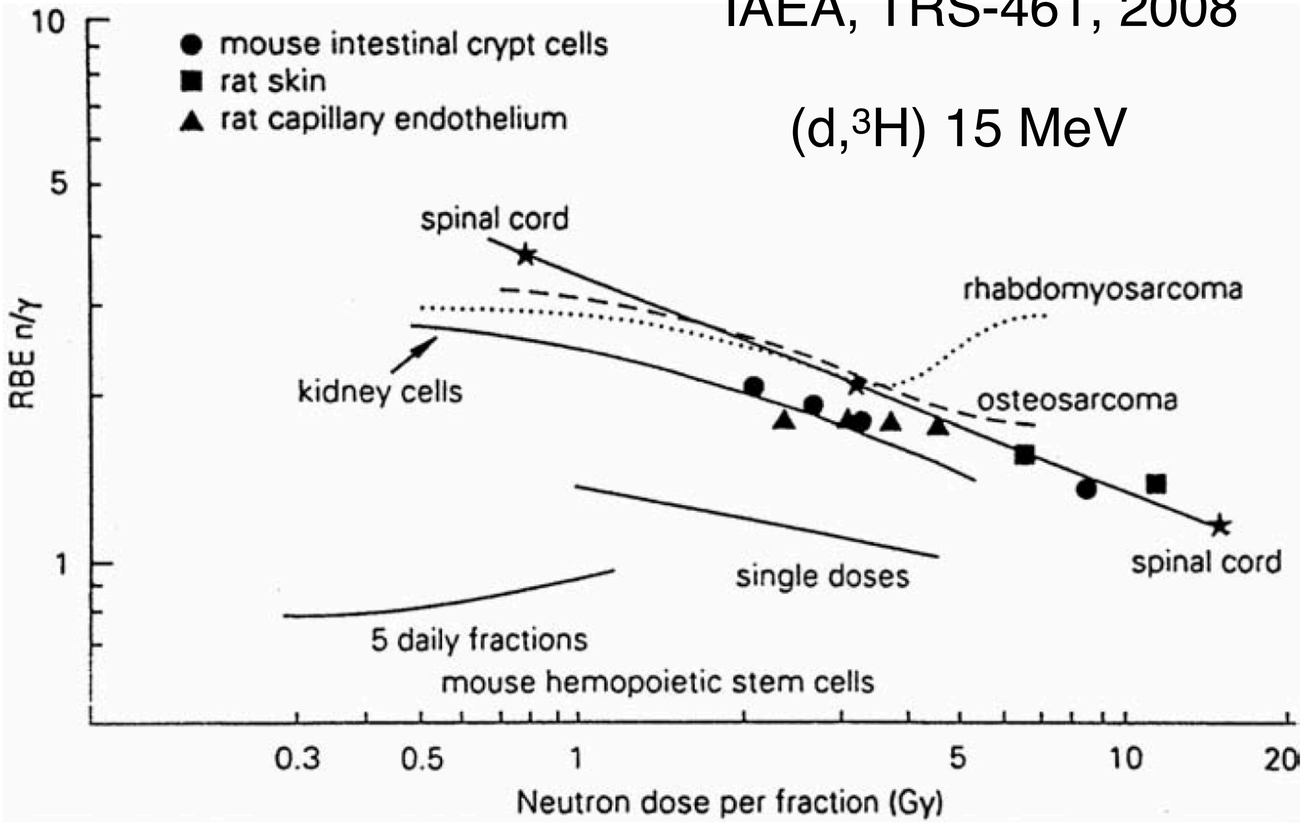

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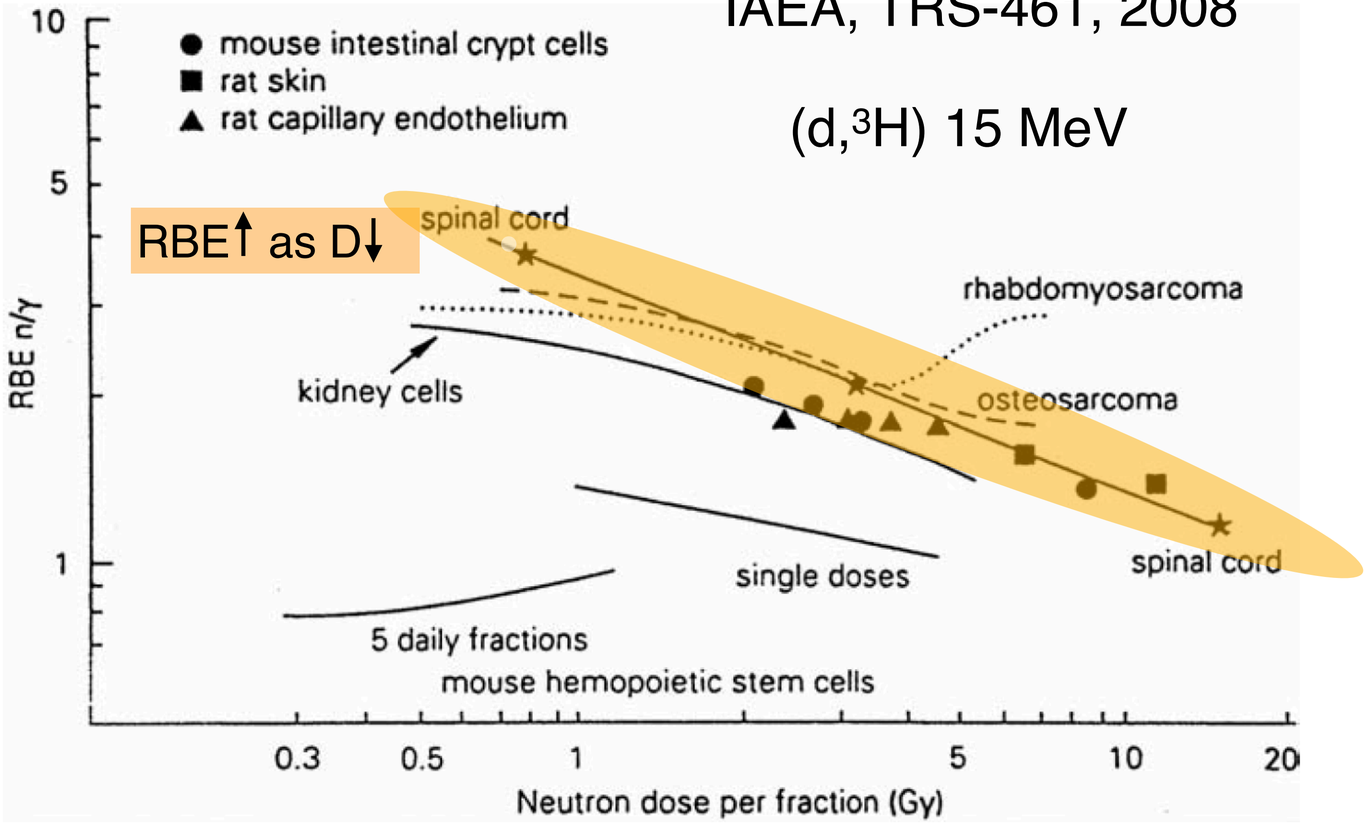

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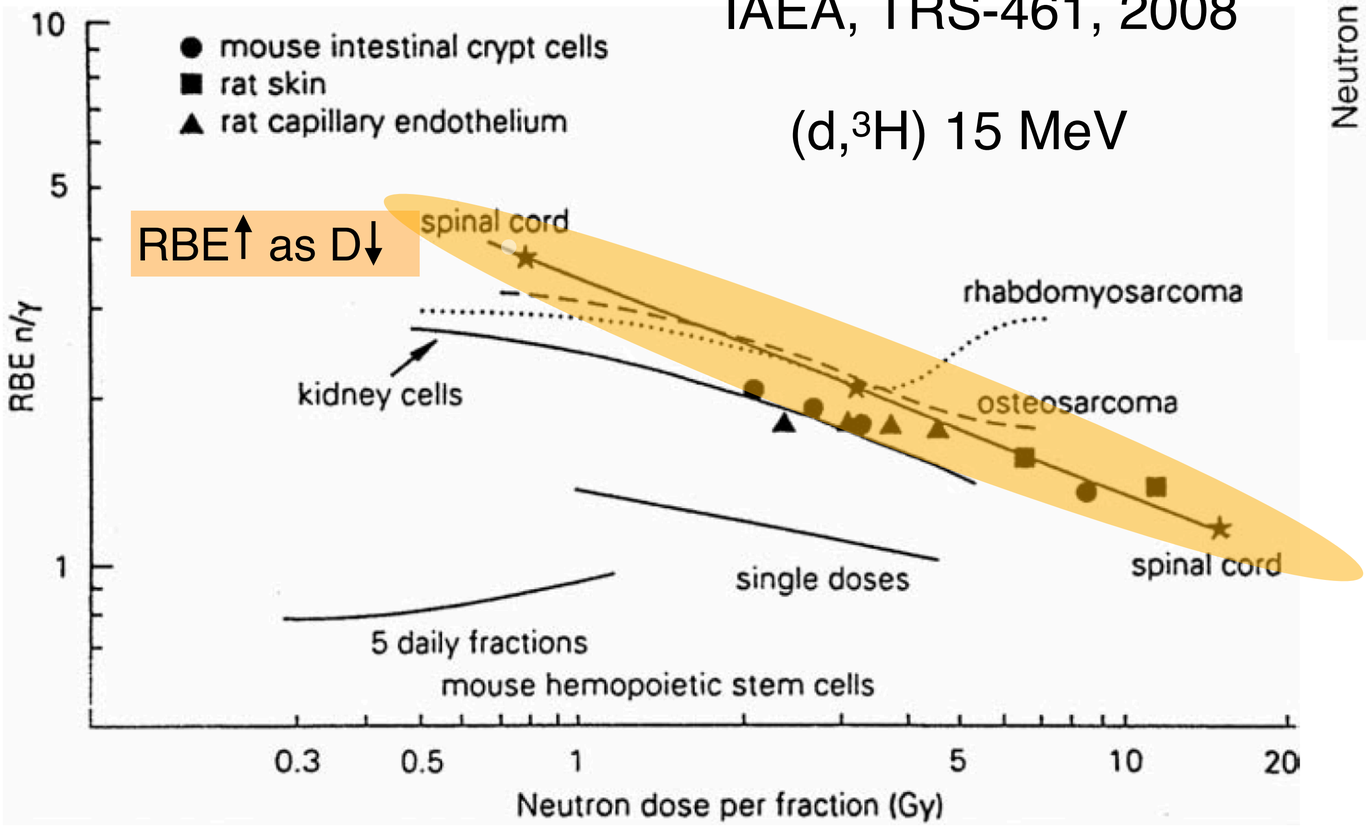

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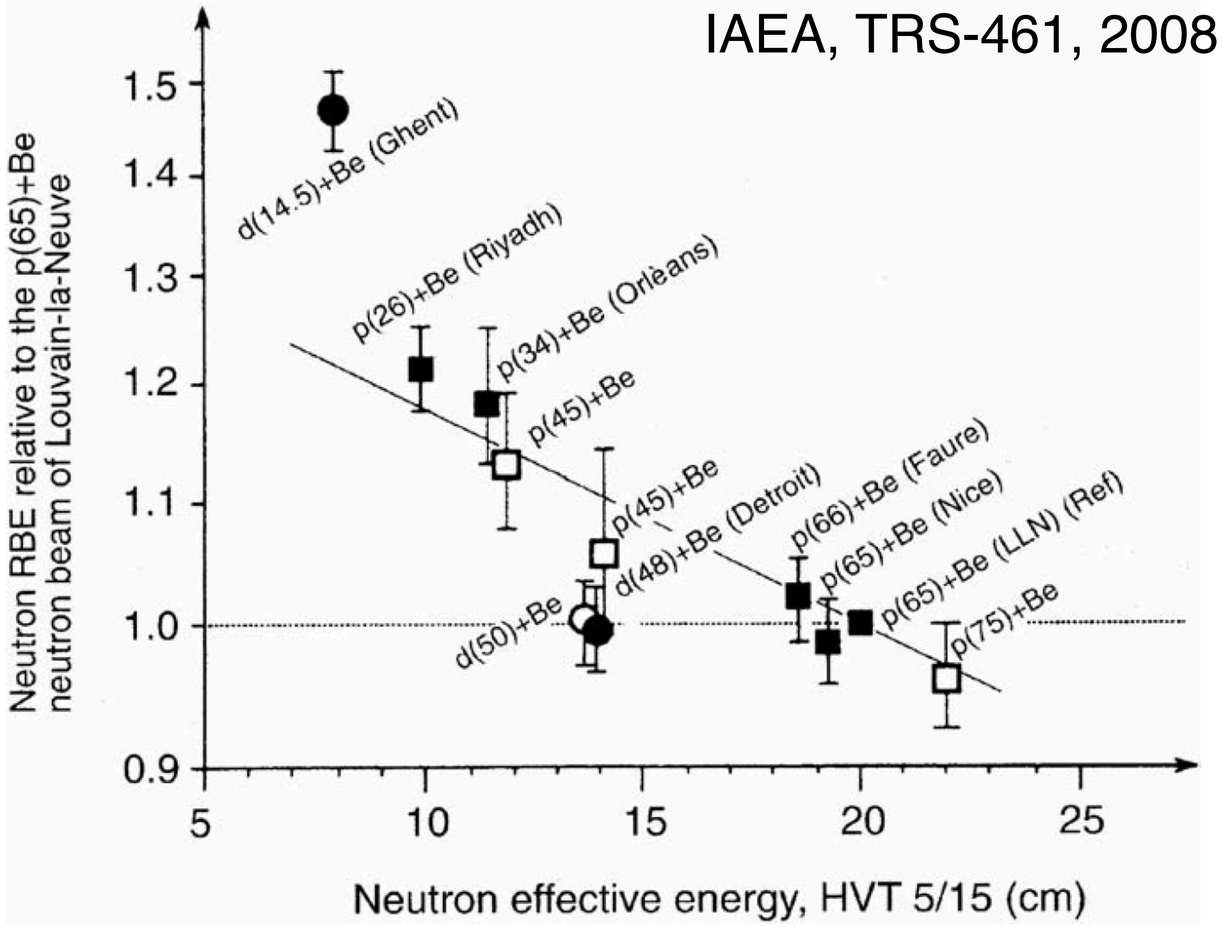

RBE of neutrons

varies significantly with **energy**
(for clinical fast neutron beams)

RBE of neutrons

- energy dependency
- Importance of calculation methods

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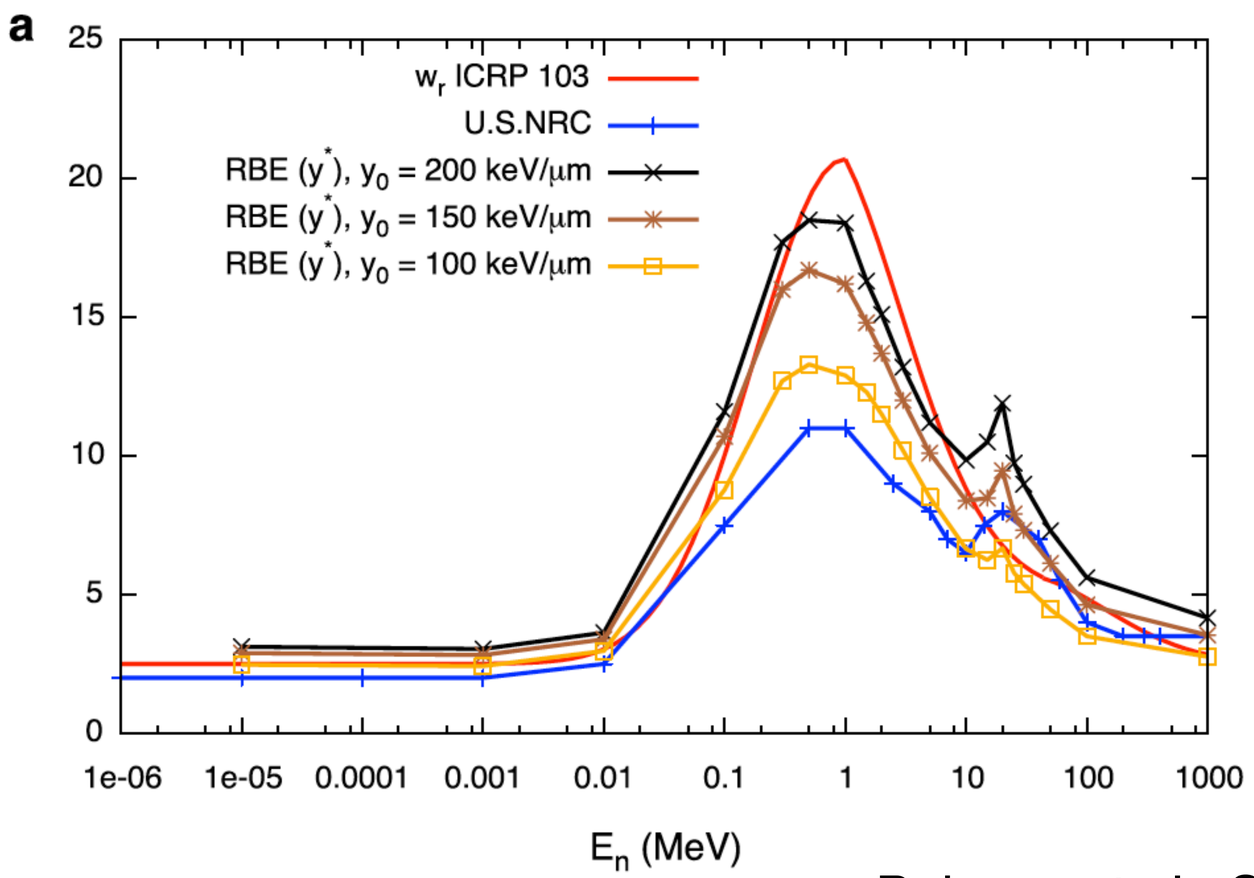
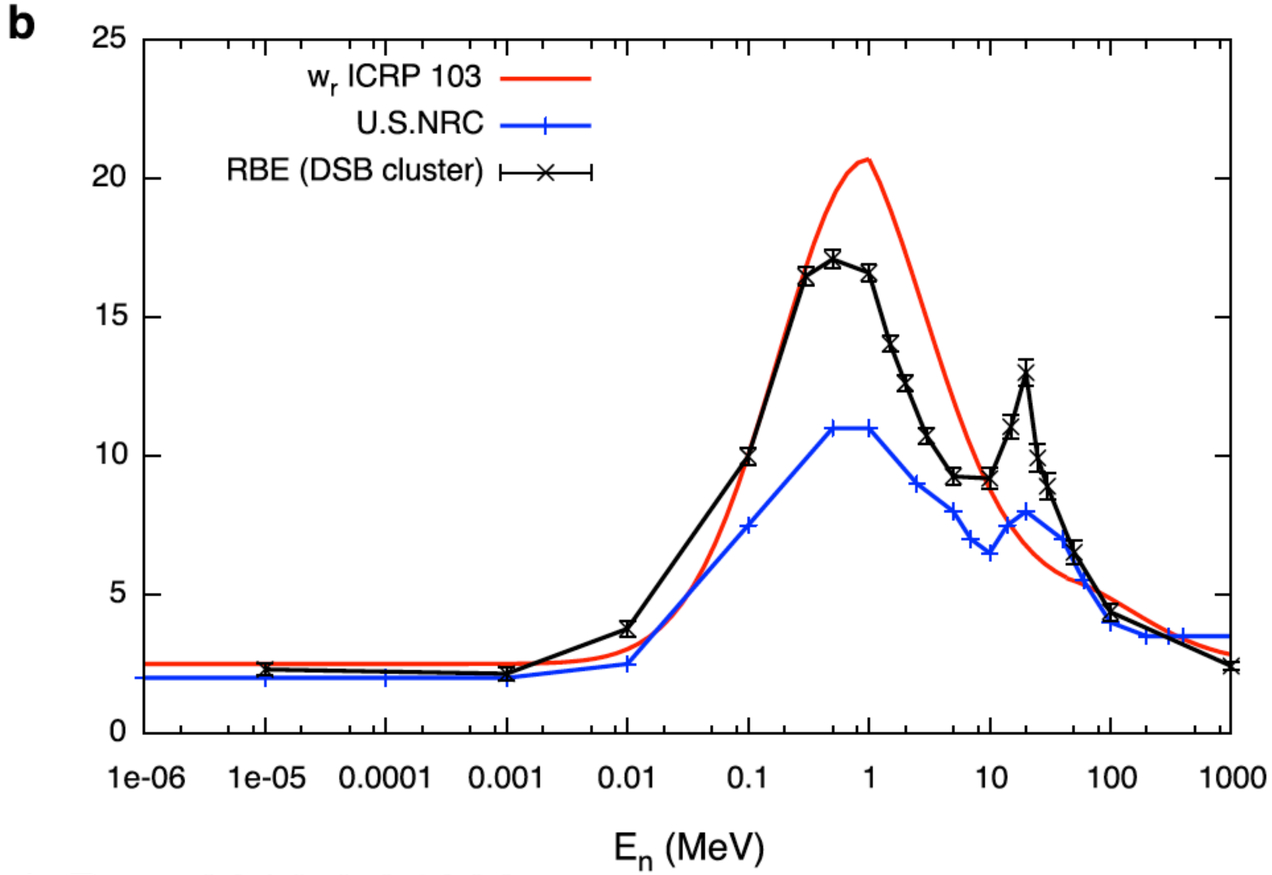
results of Monte Carlo simulations with PHITS code





Baiocco et al., Sci. Rep. 2016;6:34033

***y* = <u>lineal energy</u>** (related to LET)

the ratio of the deposited energy in a sensitive site to the mean chord length of the site

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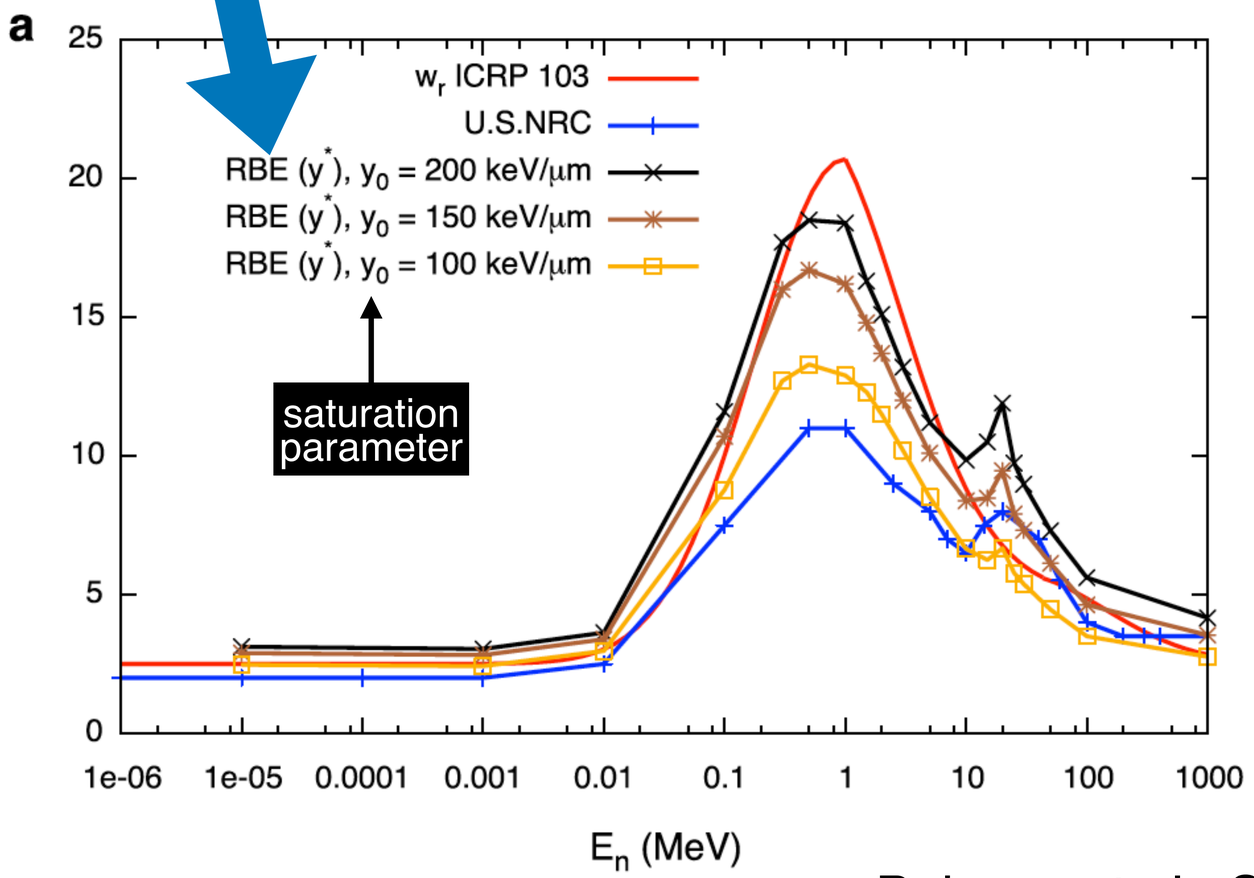

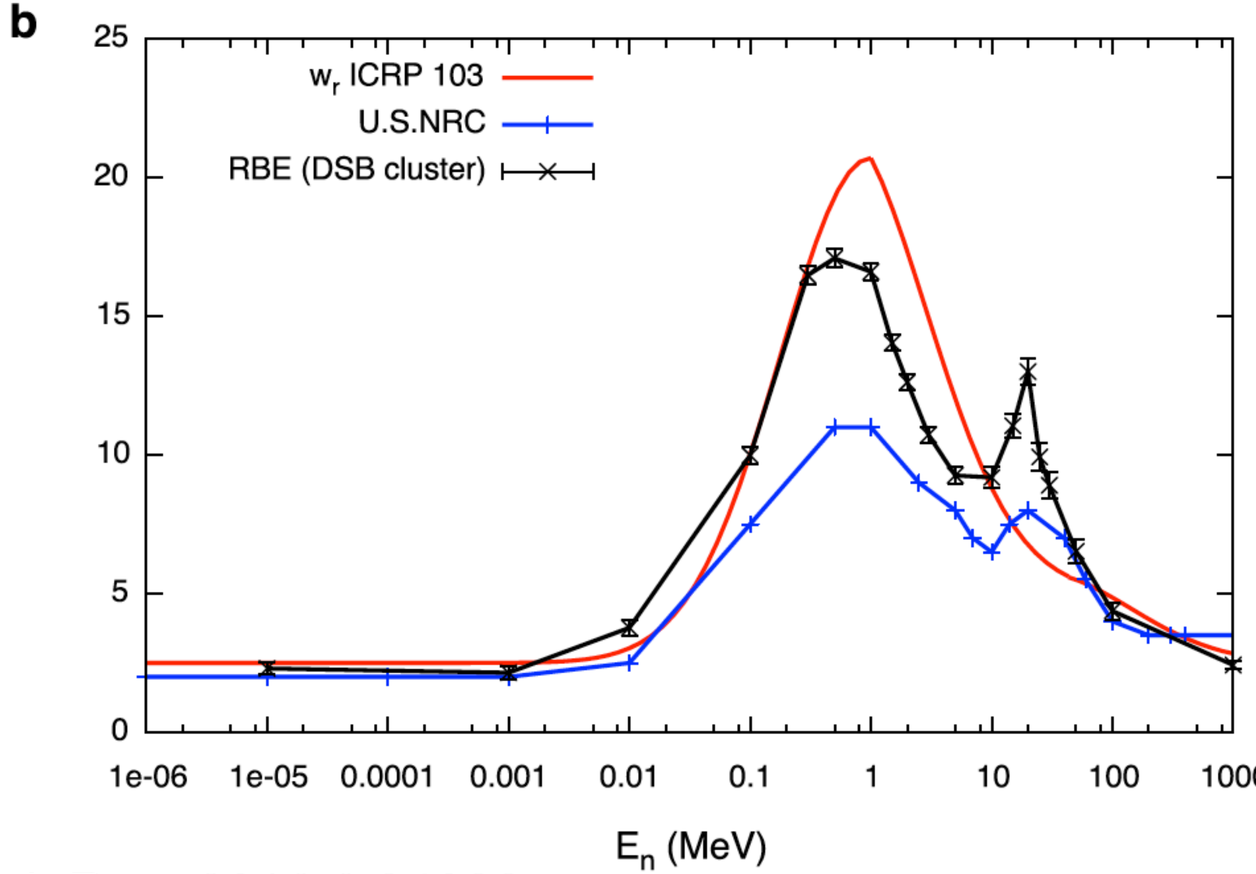

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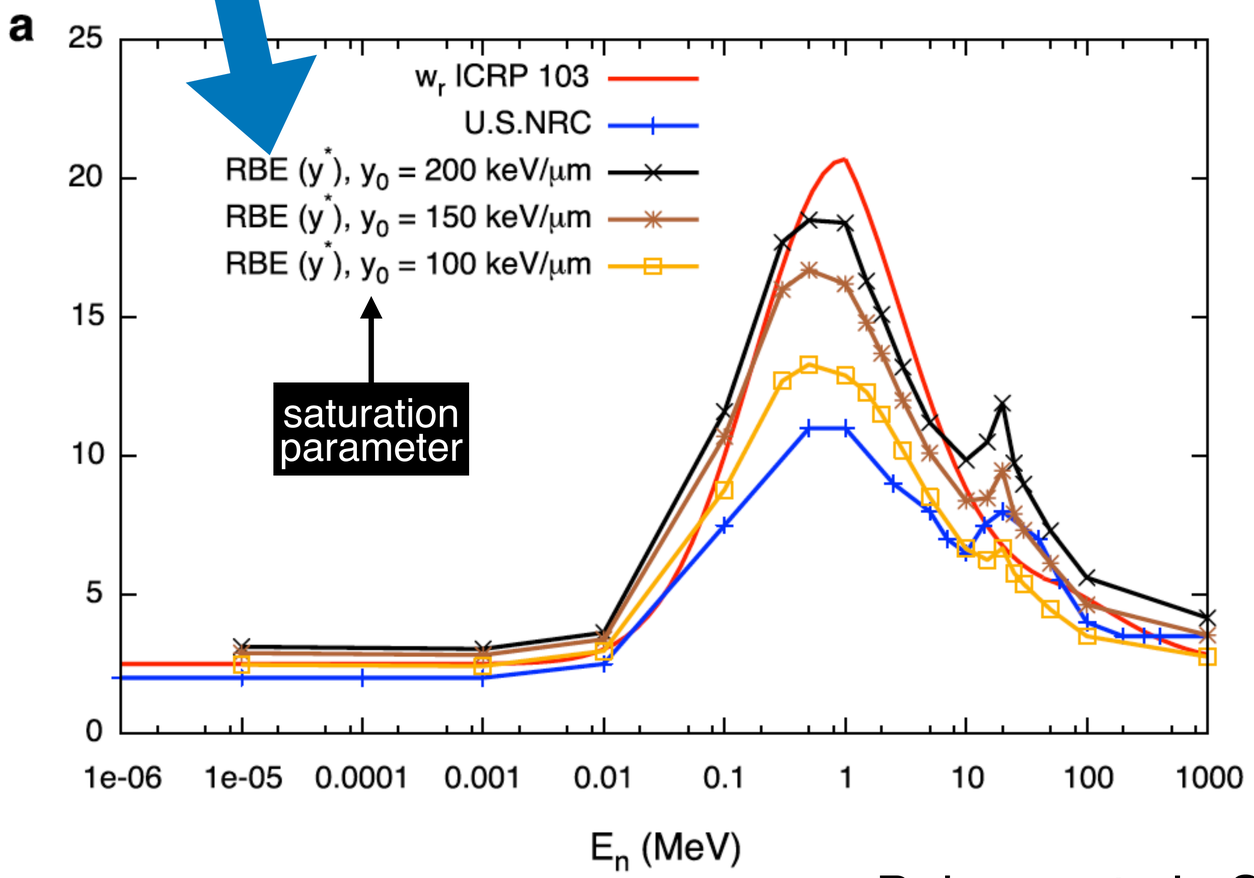

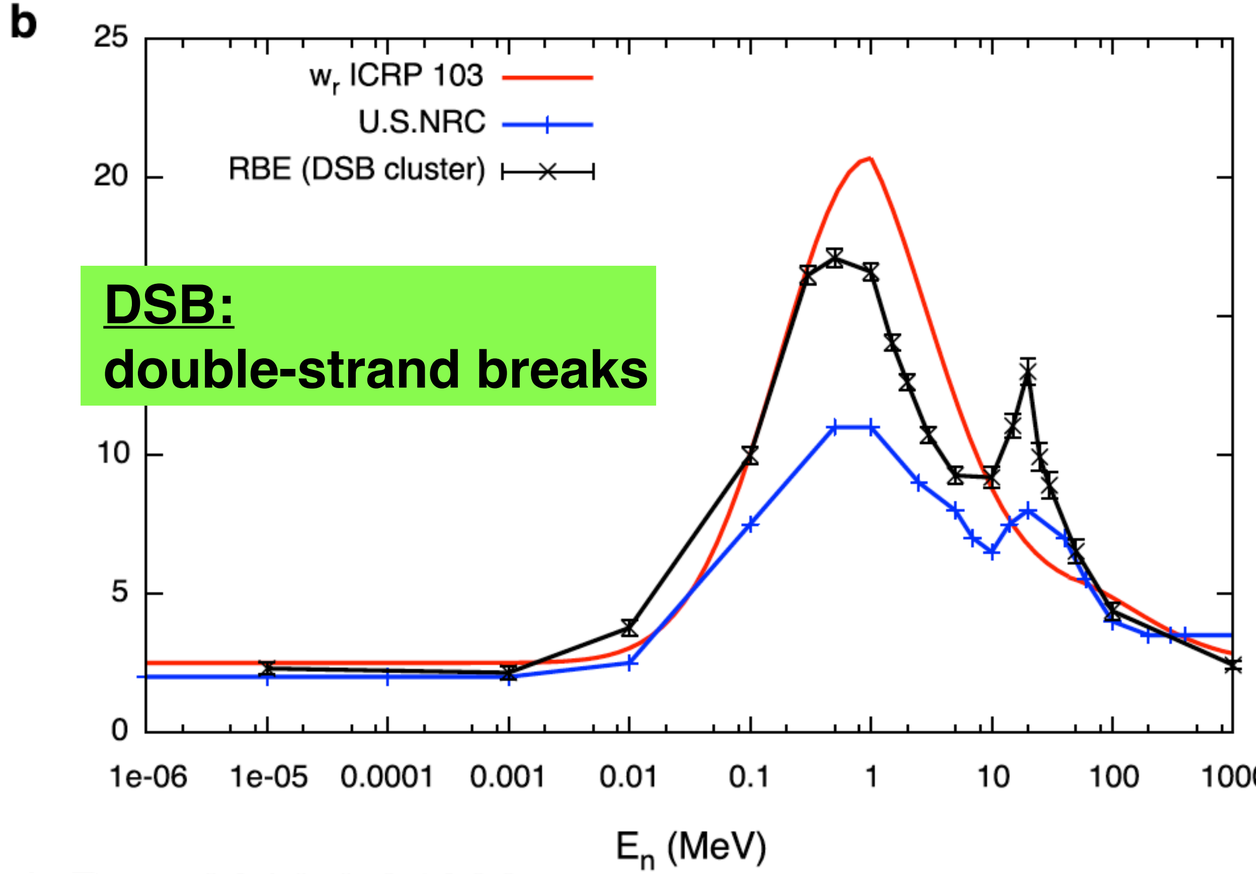

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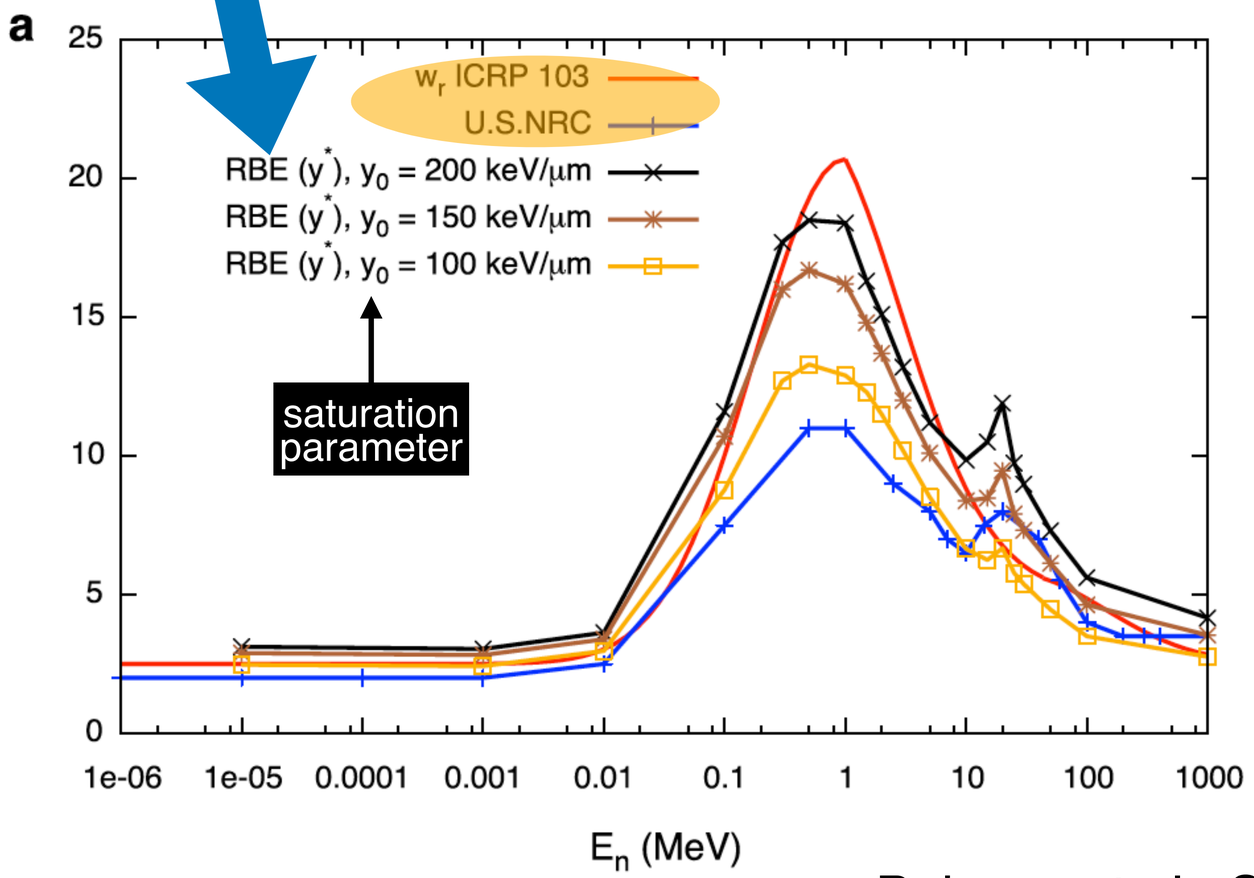

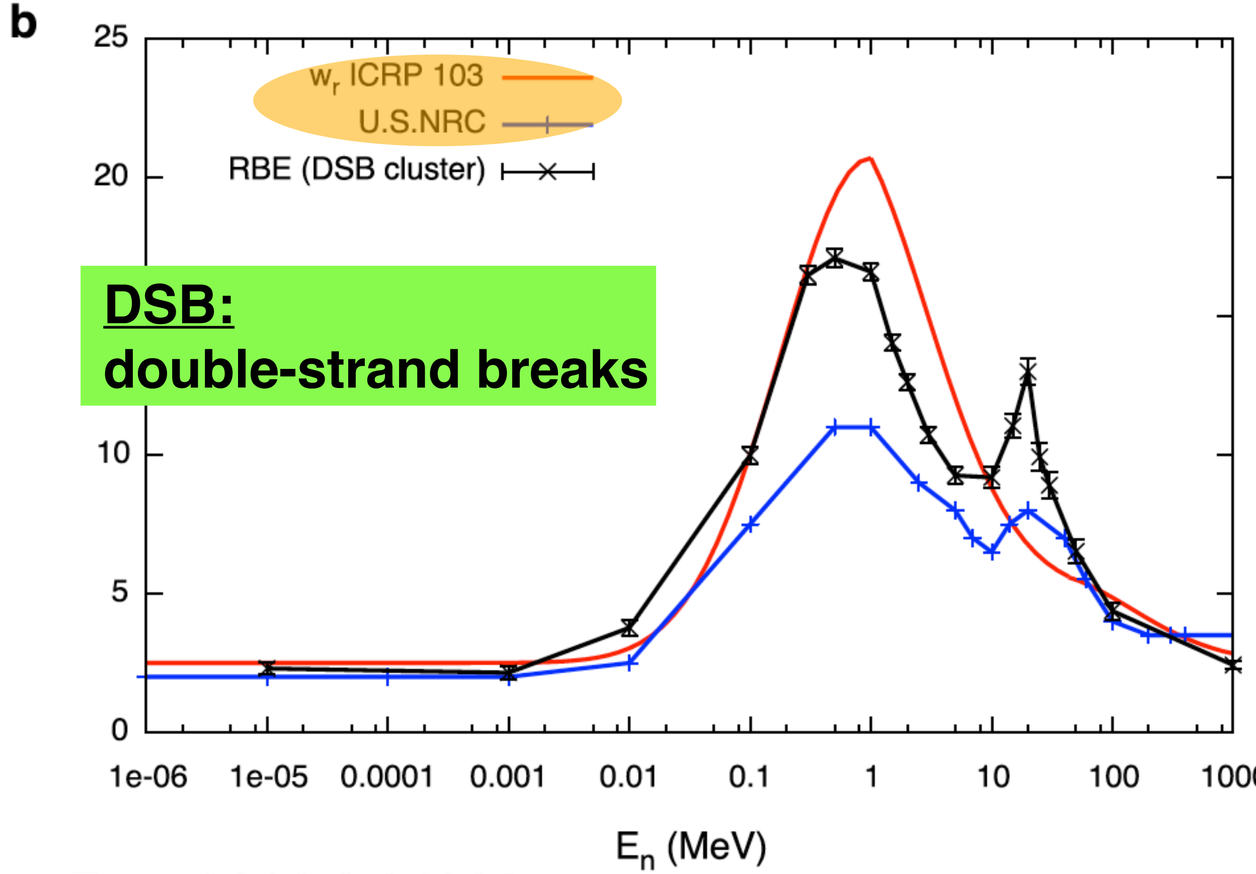

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equivalent dose in tissue T, H_T

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Type and energy range[2]	Radiation weighting factor, w_R
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Electrons and muons, all energies[3]	1
Neutrons, energy < 10 keV	5
10 keV to 100 keV	10
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(See also Figure 1)	
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Alpha particles, fission fragments, heavy nuclei	20

what about w_R?

chosen by ICRP

$w_R = 1$ for low LET radiations

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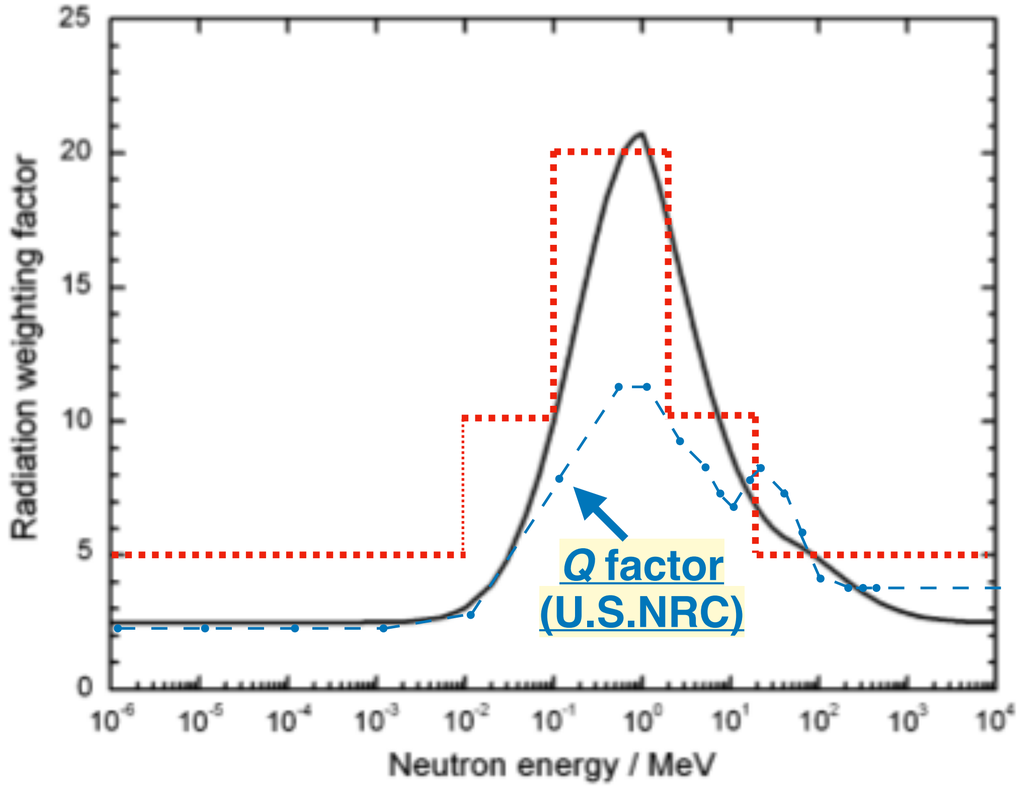
ICRP 60 (1991)



$$w_R = \begin{cases} 2.5 + 18.2e^{-[\ln(E_n)]^2/6}, & E_n < 1 \text{ MeV} \\ 5.0 + 17.0e^{-[\ln(2E_n)]^2/6}, & 1 \text{ MeV} \leqslant E_n \leqslant 50 \text{ MeV} \\ 2.5 + 3.25e^{-[\ln(0.04E_n)]^2/6}, & E_n > 50 \text{ MeV} \end{cases}$$

ICRP 103 (2007)

neutron radiobiology? since when?

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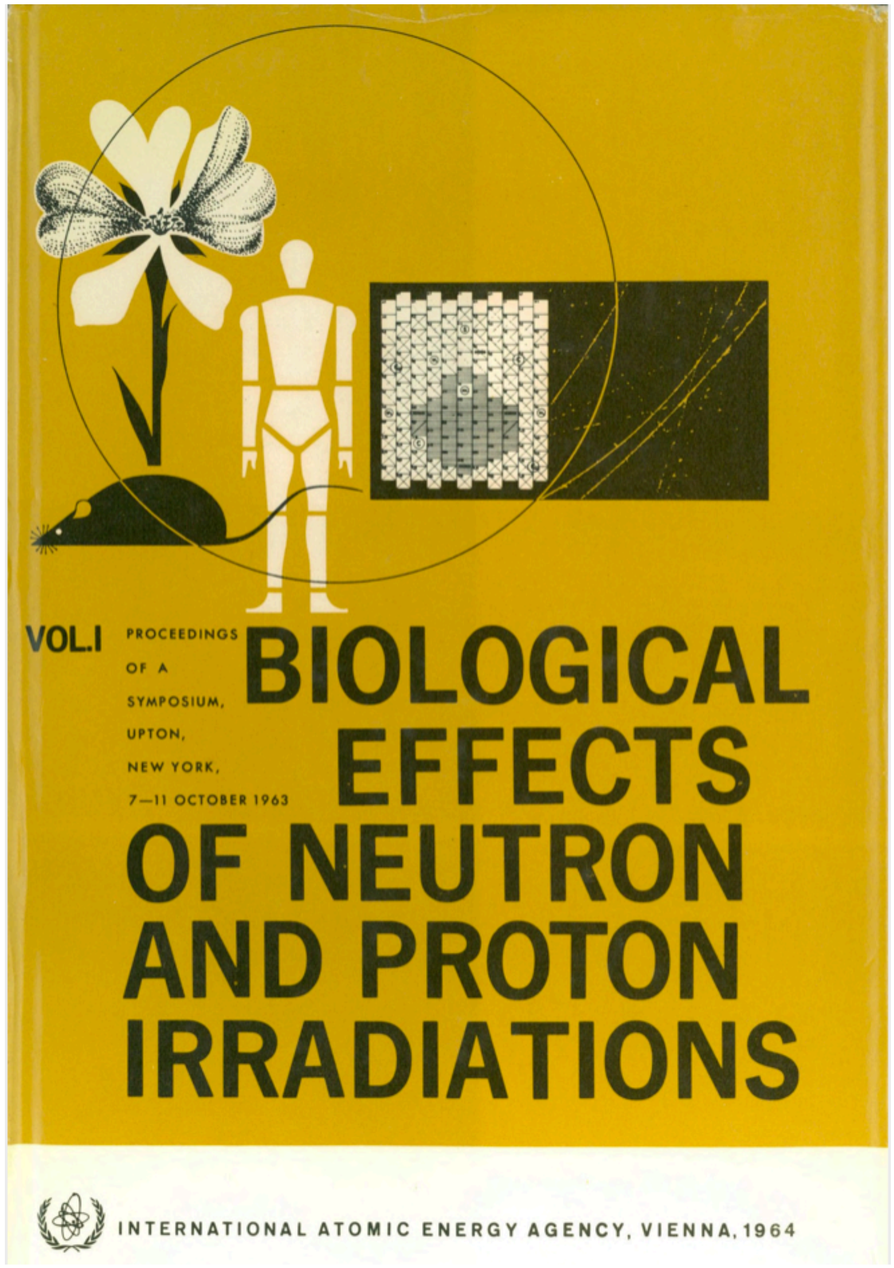

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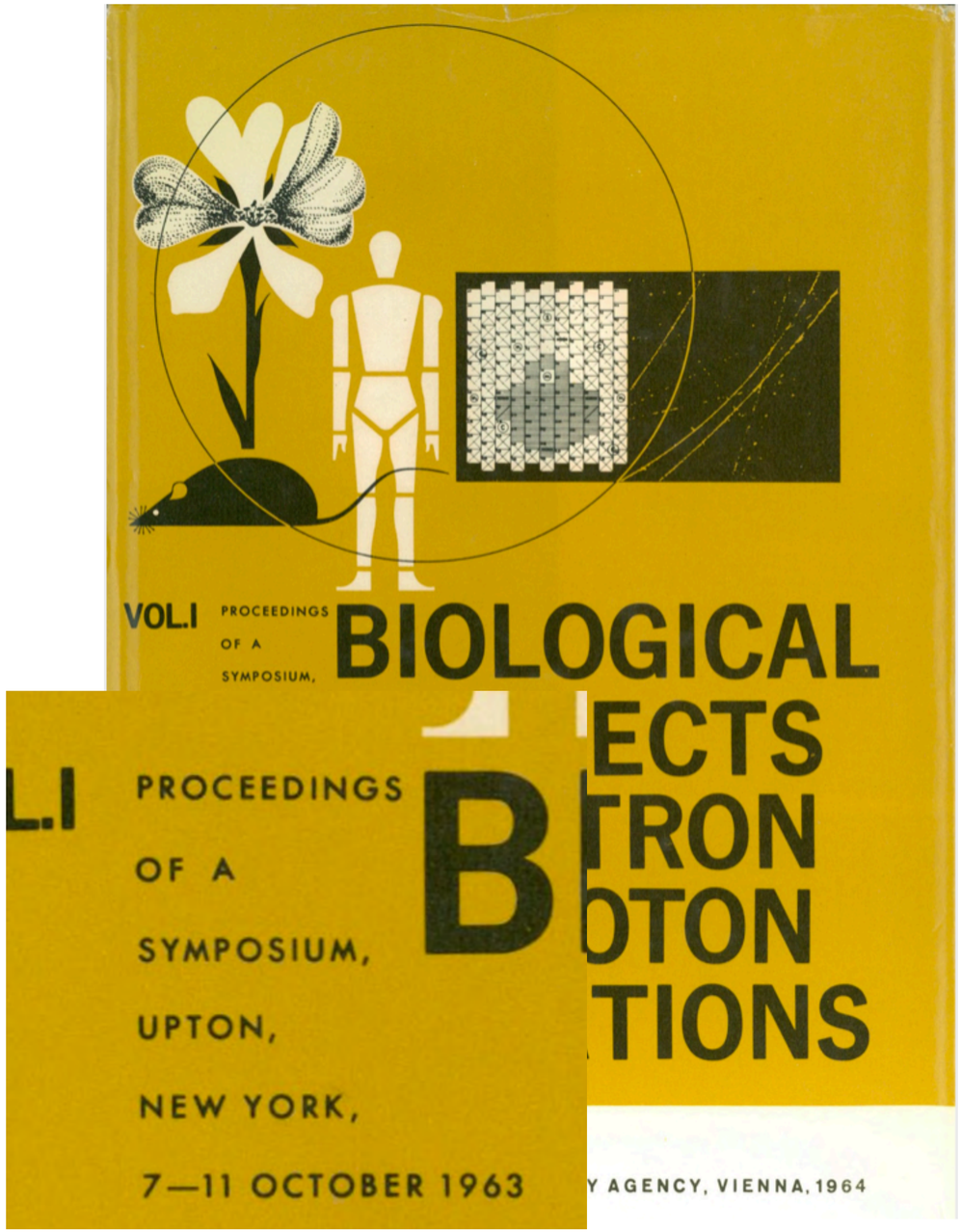

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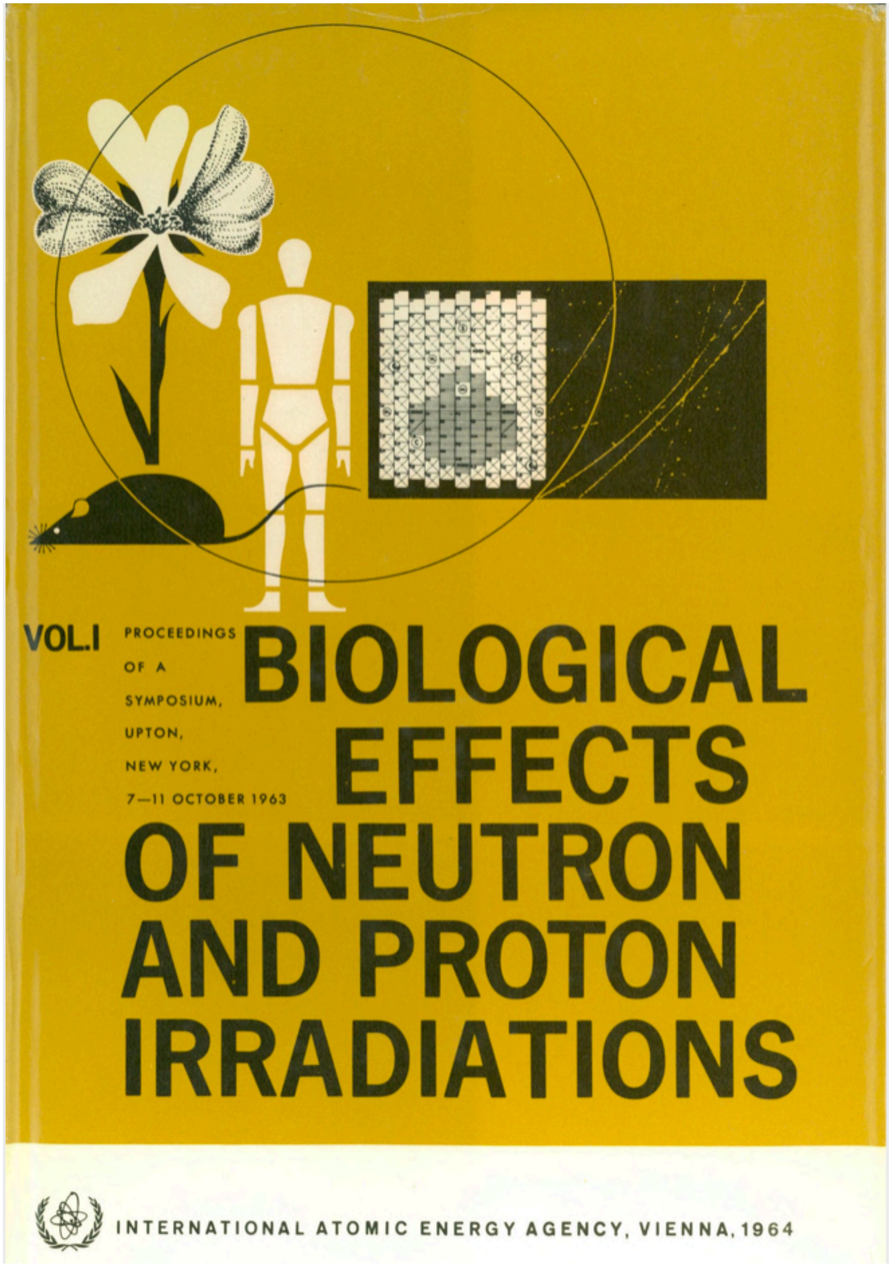

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The two volumes contain papers on the following subjects: 1. Dosimetry, estimation of absorbed dose of neutrons in biological material; 2. Biological effects of high-energy protons; 3. Cellular and genetic effects; 4. Pathology of neutron irradiation, including acute and chronic radiation syndromes (mortality, anatomical and histological changes, biochemical and metabolic disturbances) and delayed consequences; 5. Relative biological effectiveness of neutrons evaluated by different biological tests. At the end of Vol. II a panel discussion on biophysical considerations in neutron experimentation is presented.

Papers are in their original languages (44 English, 4 French and 6 Russian); each abstract is in English, French, Russian and Spanish; discussions and panel discussions are in English.

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(1964)

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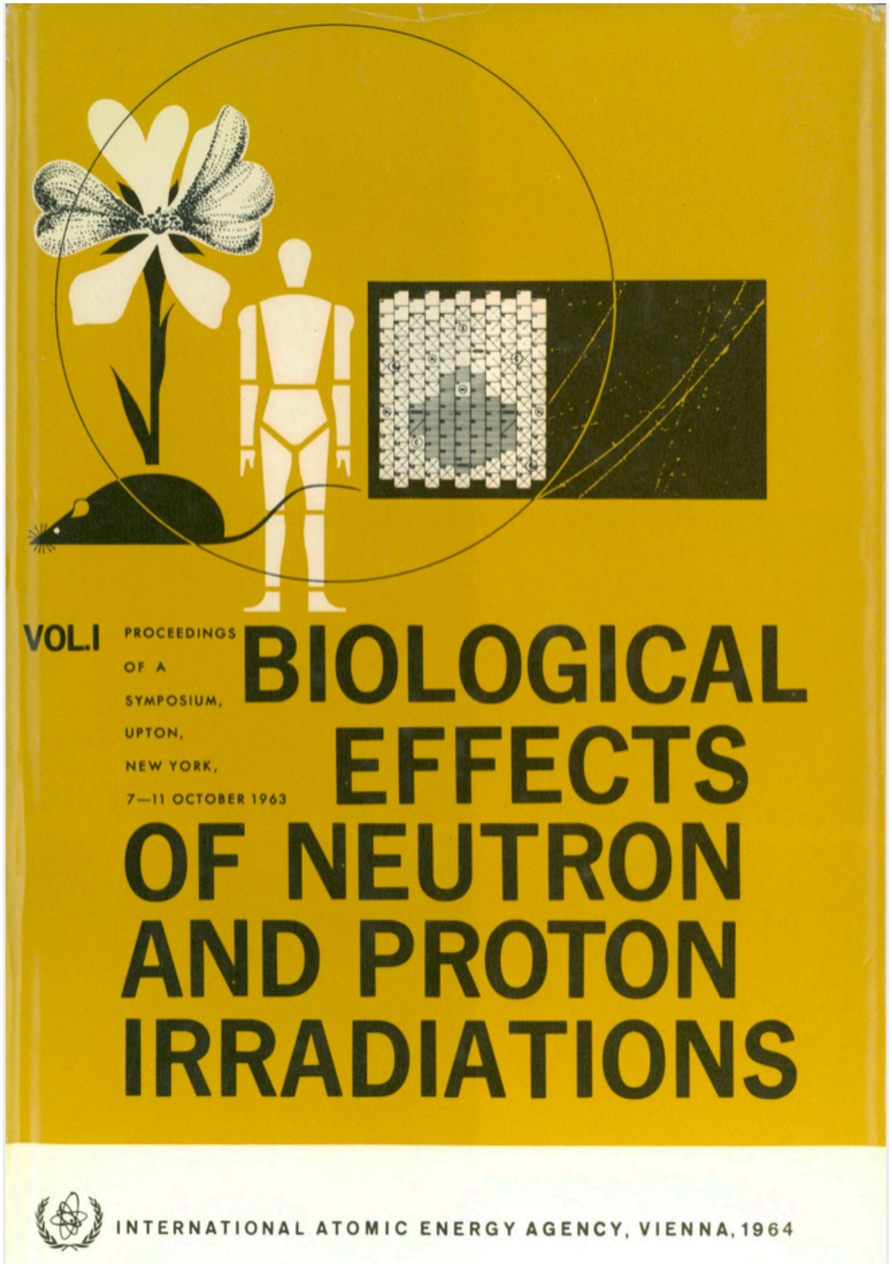

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Survival of cultured human cells after irradiation with fast neutrons of different energies in hypoxic and oxygenated conditions†

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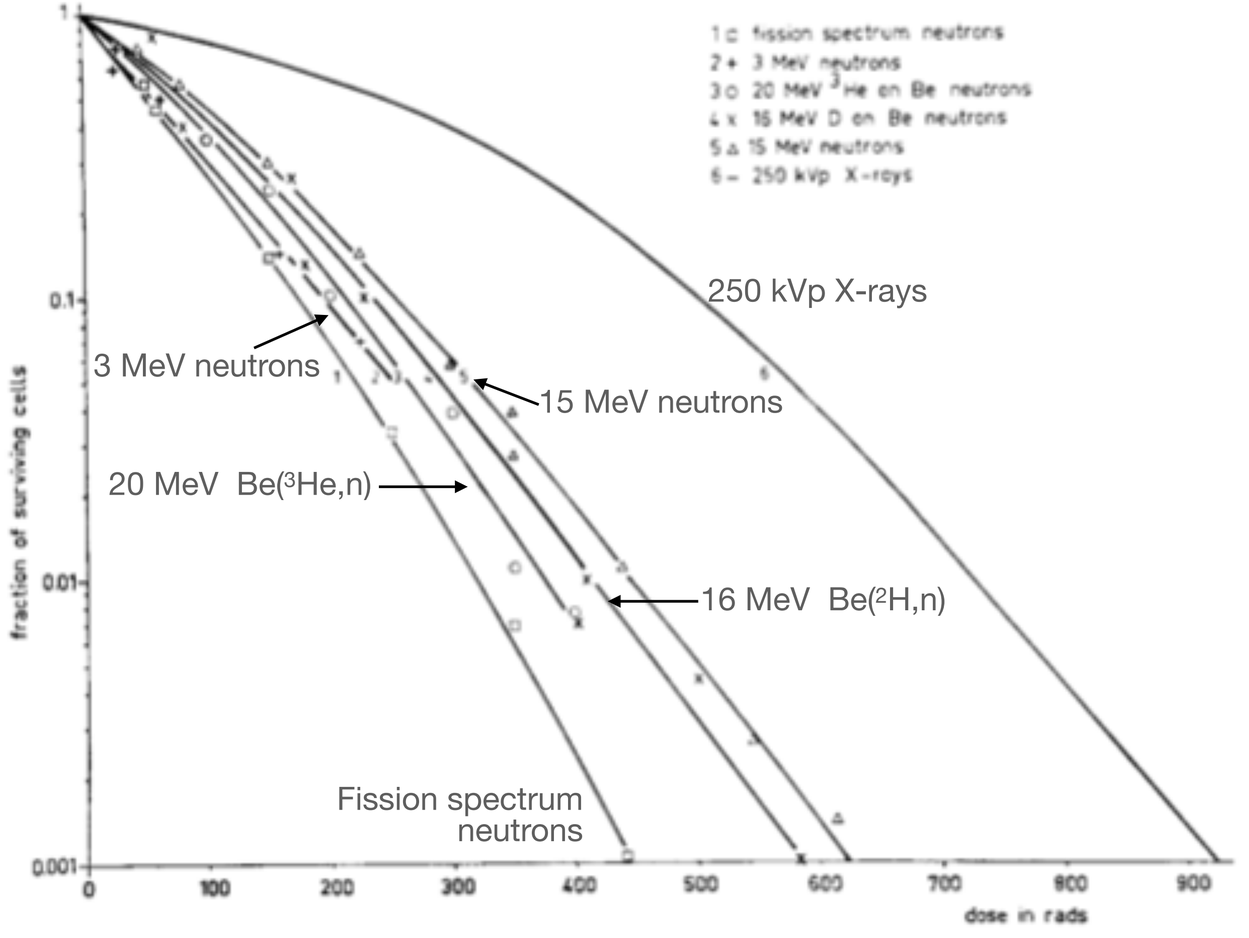

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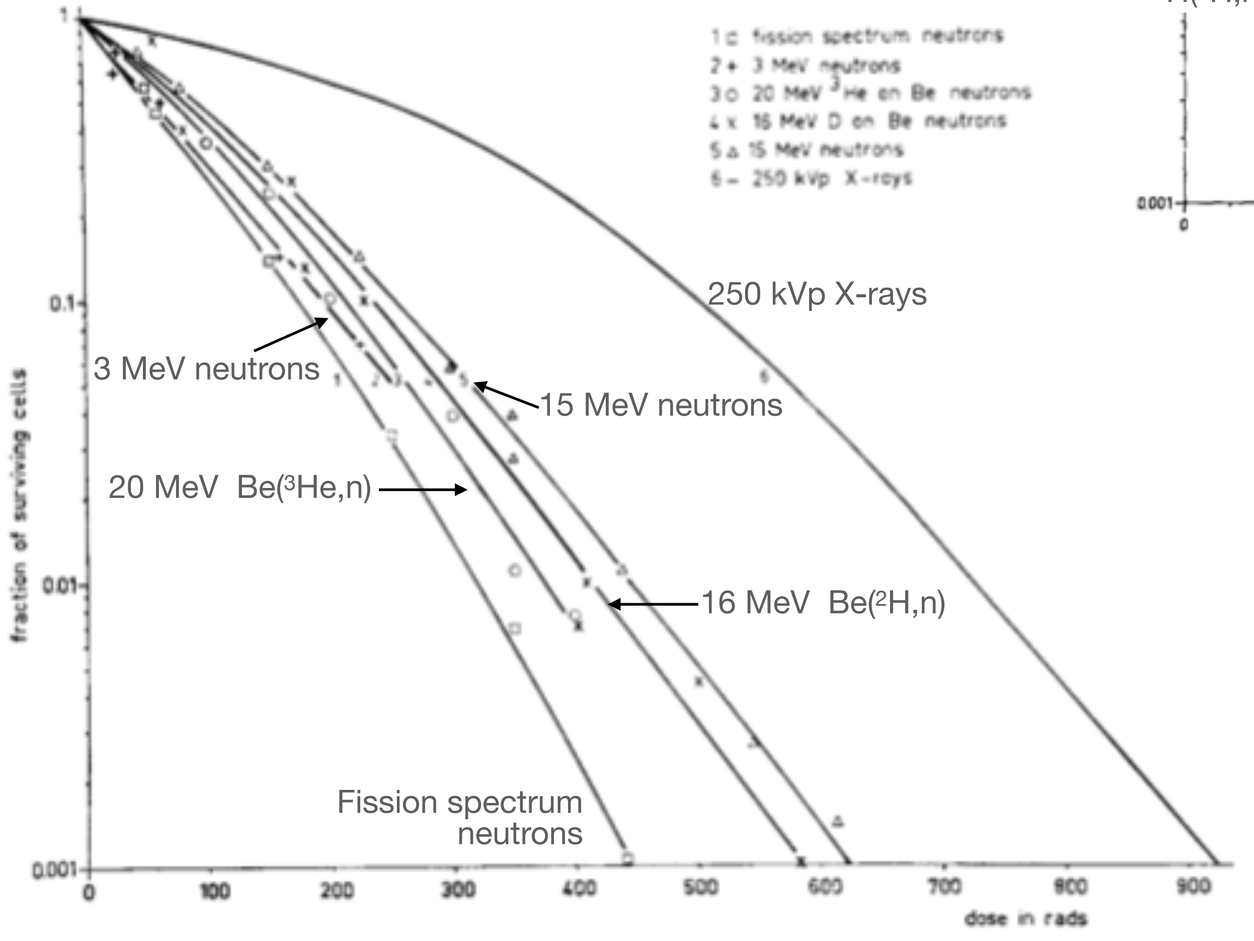

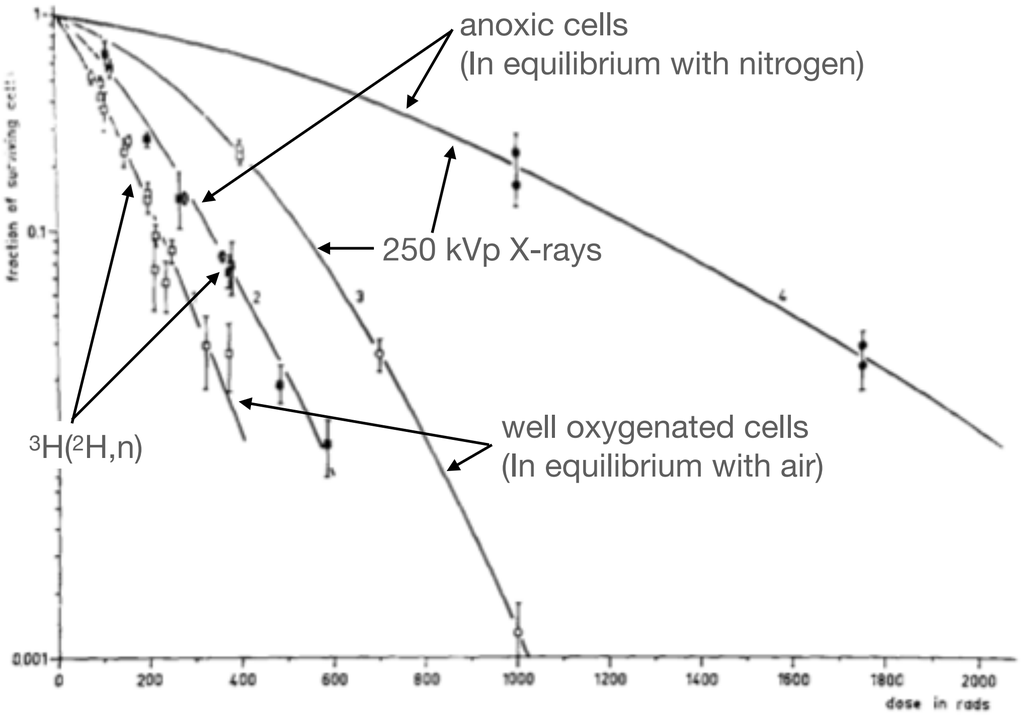

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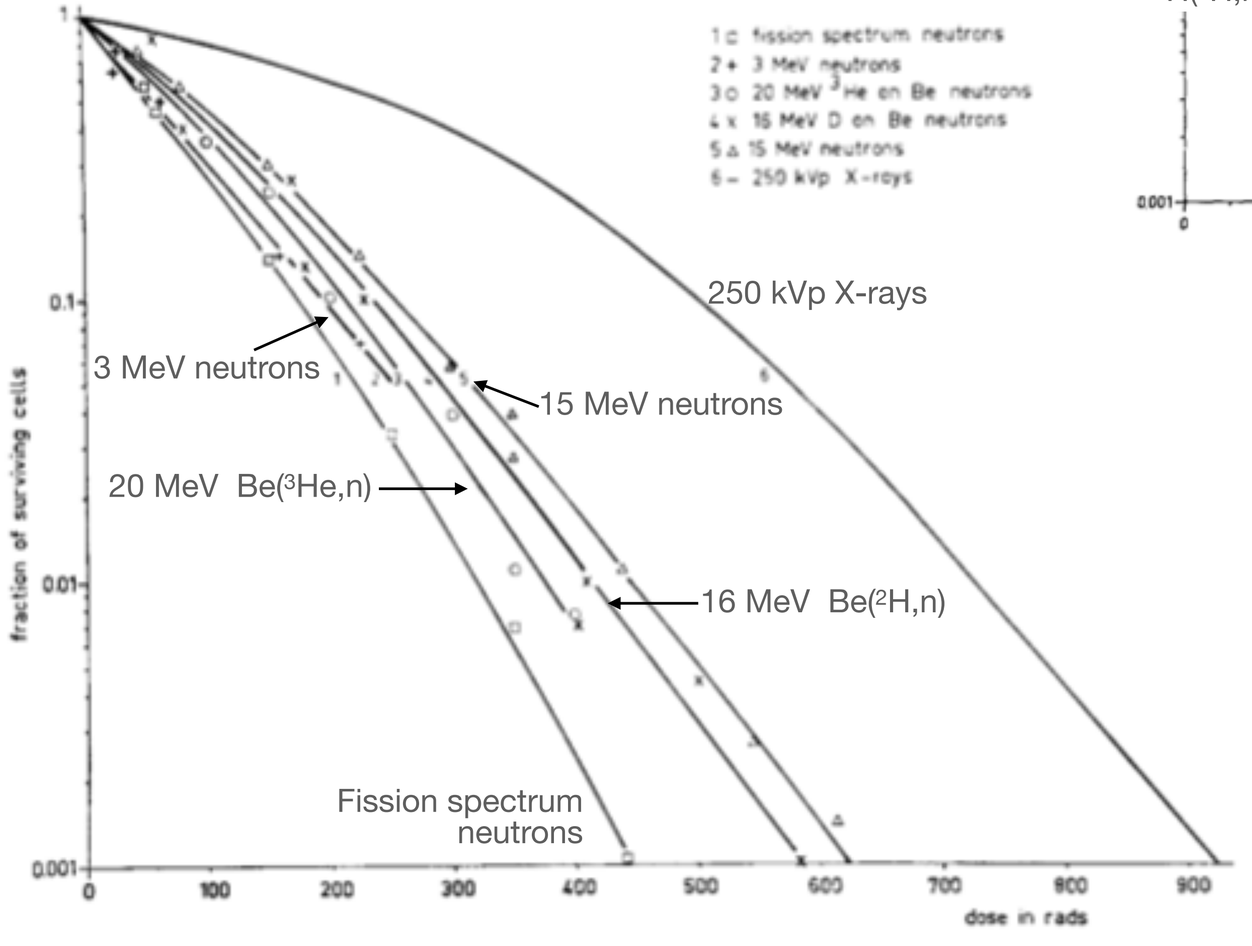
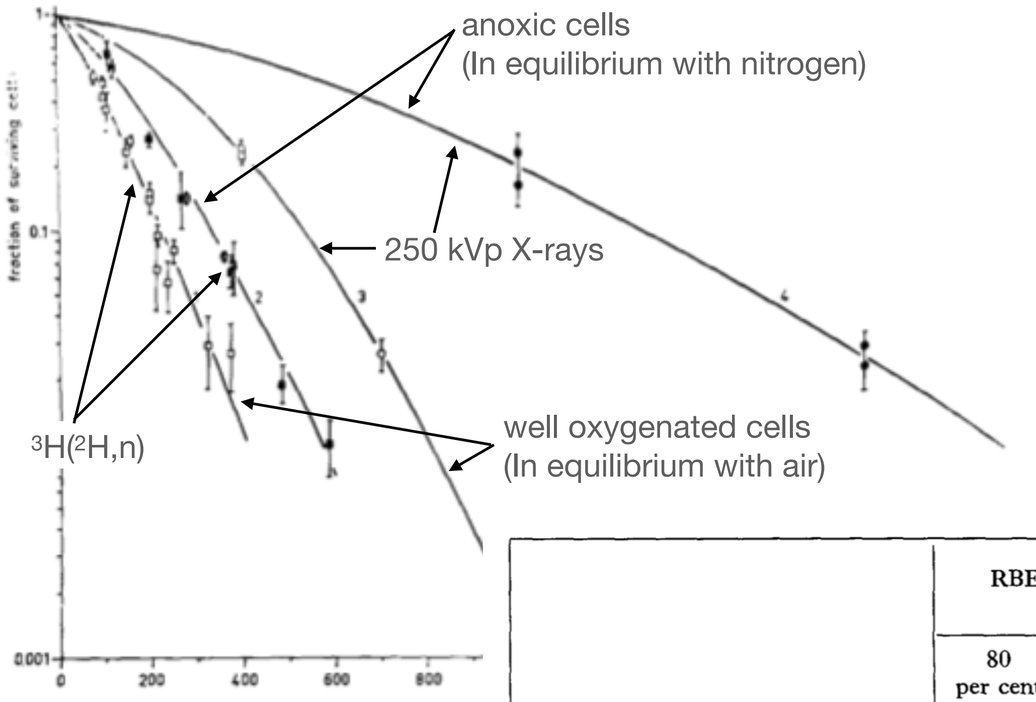
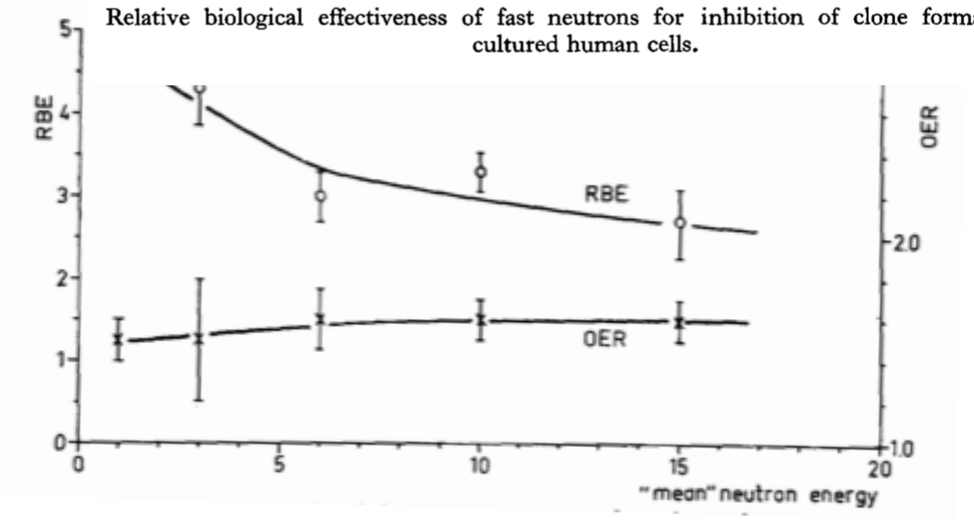




	RBE-values at different percentages survival			
	80 per cent	20 per cent	5 per cent	1 per cent
D–T neutrons	2·9	2·2	1·8	1·6
16 MeV D on Be neutrons	3·6	2·4	2·0	1·8
20 MeV ³He on Be neutrons	4·2	2·7	2·2	1·9
D–D neutrons	5·0	3·1	2·3	2·0
Fission spectrum neutrons	6·1	3·4	2·6	2·3

Relative biological effectiveness of fast neutrons for inhibition of clone formation by cultured human cells.



Acta Oncologica Vol. 33, No. 3, pp. 233–240, 1994

NEUTRON RADIOBIOLOGY REVISITED

JULIANA DENEKAMP

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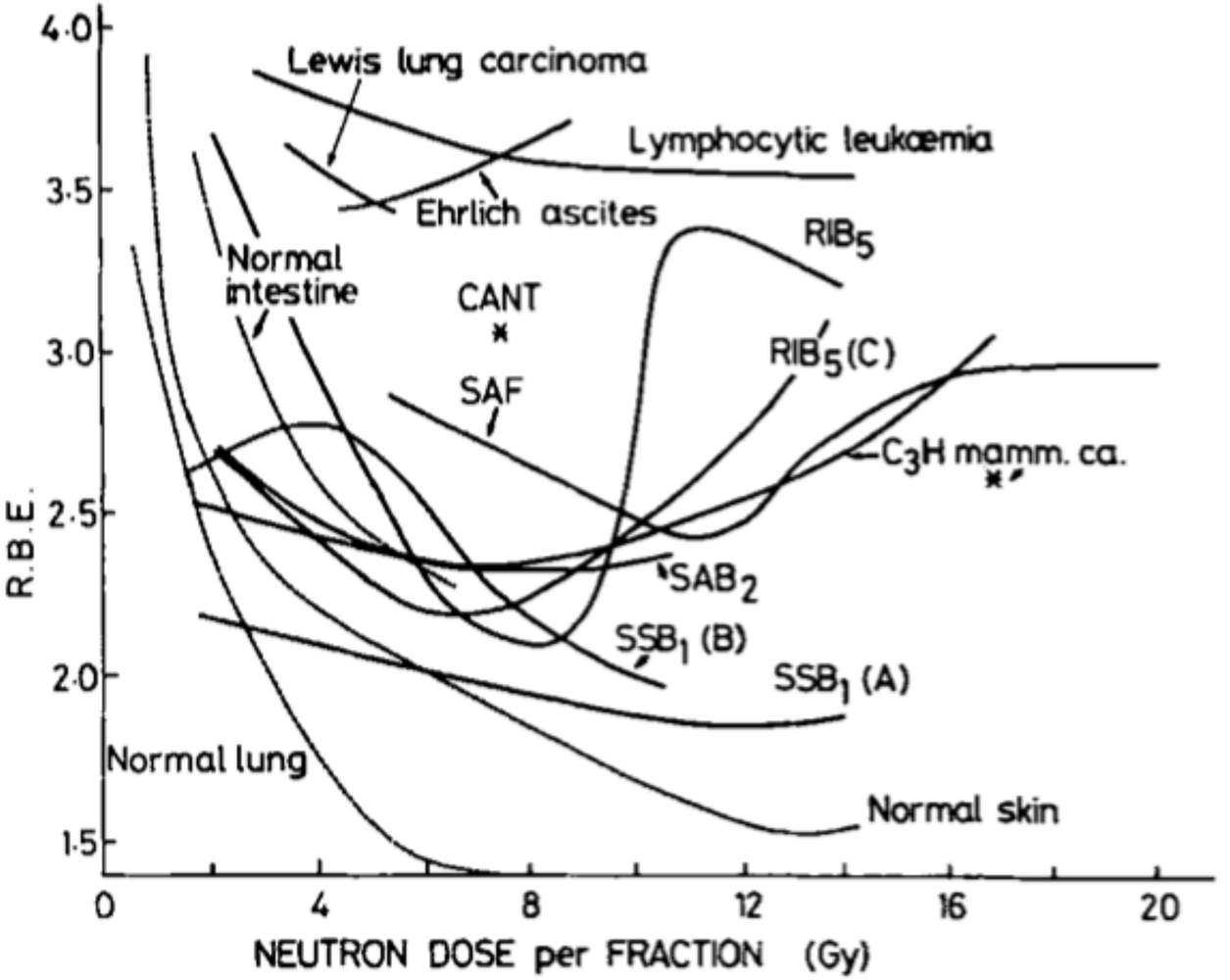

Fig. 2. Summary of RBE values compiled by S.B. Field (pers. comm.) for a range of normal tissues and tumours. The normal tissues showed the expected decrease in RBE at higher doses but the tumours showed more complex curves with a strikingly higher range of RBE values than for skin at doses above 10 Gy per fraction.

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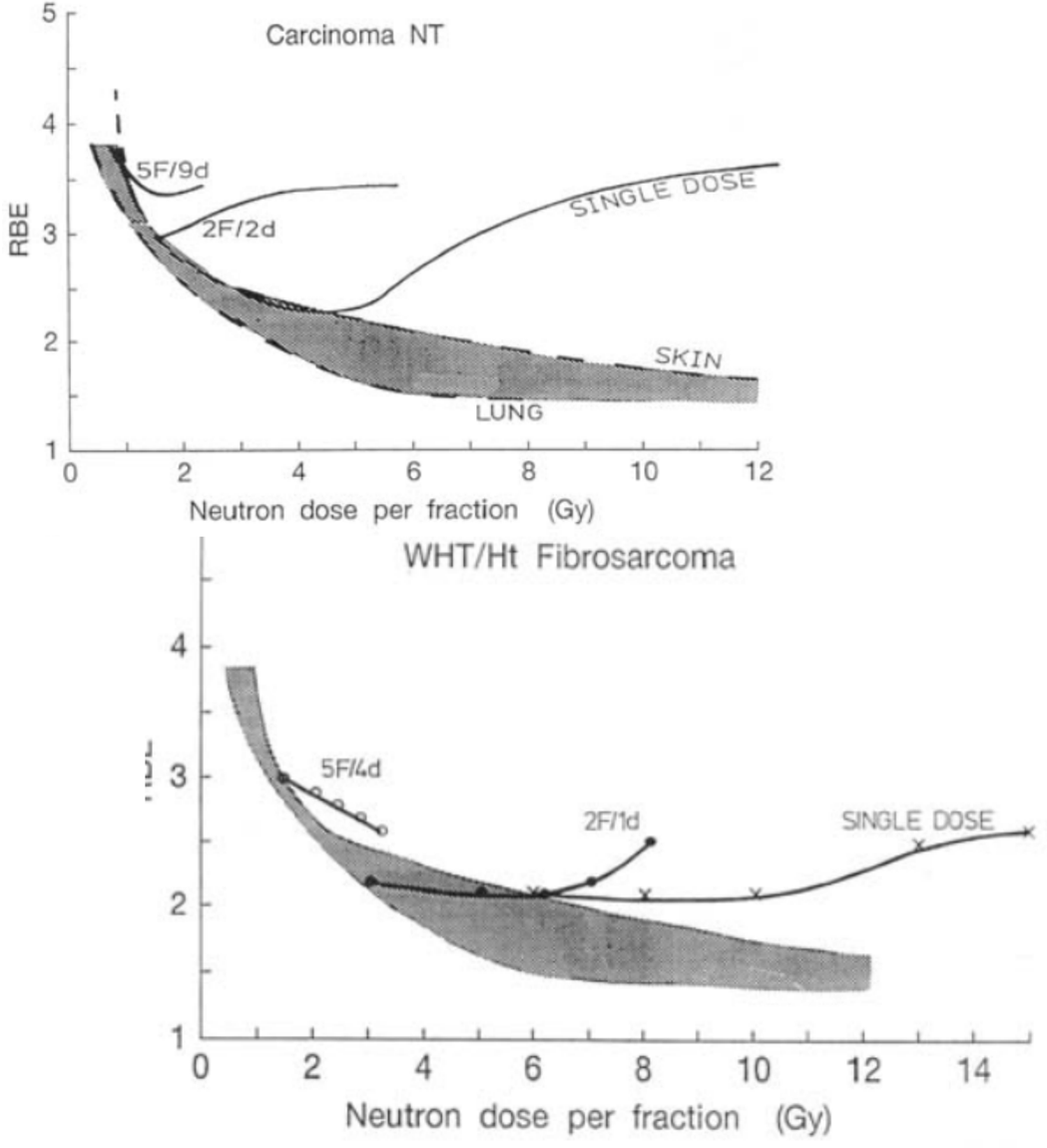

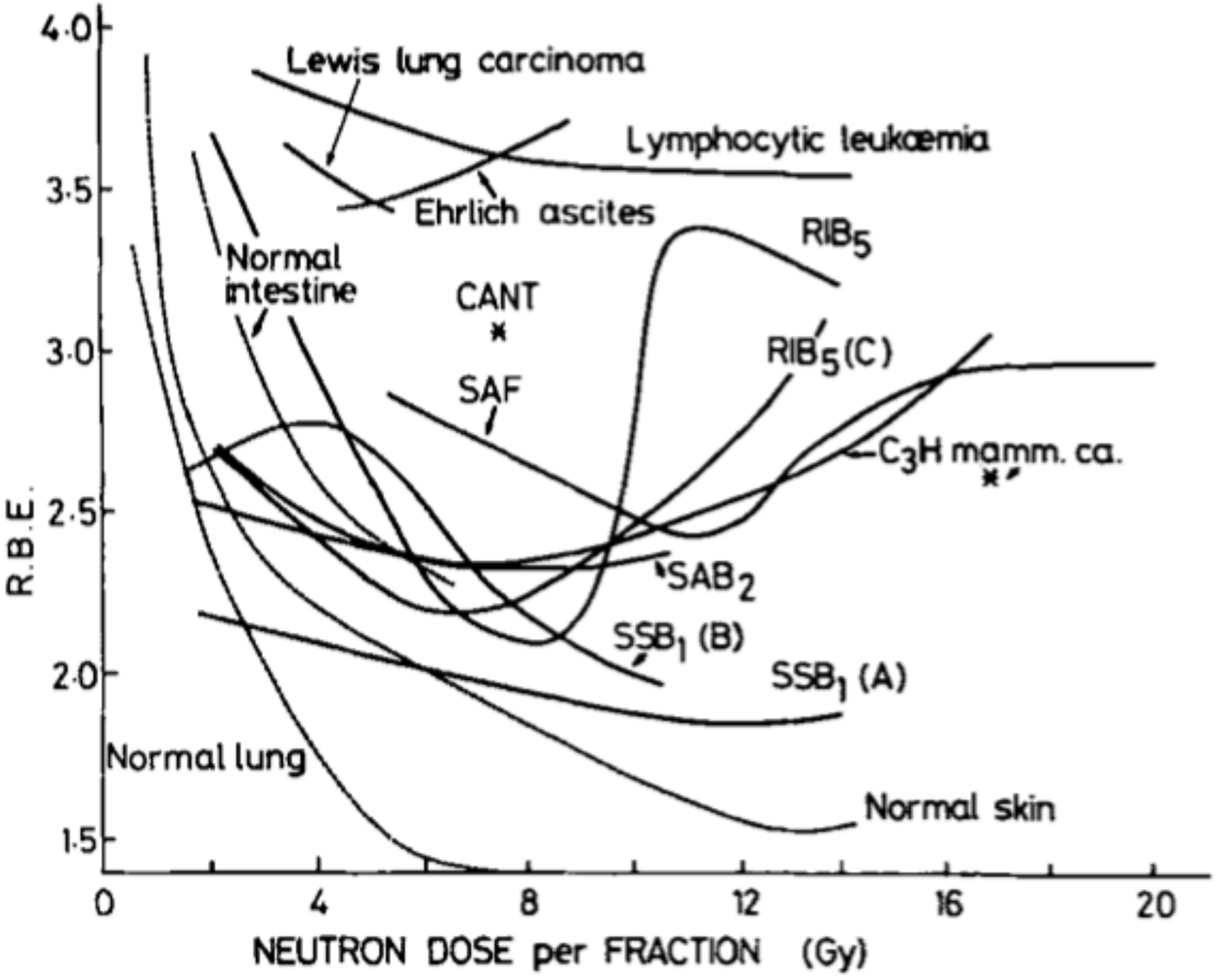

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The British Journal of Radiology, 84 (2011), S11–S18

Fast neutron relative biological effects and implications for charged particle therapy

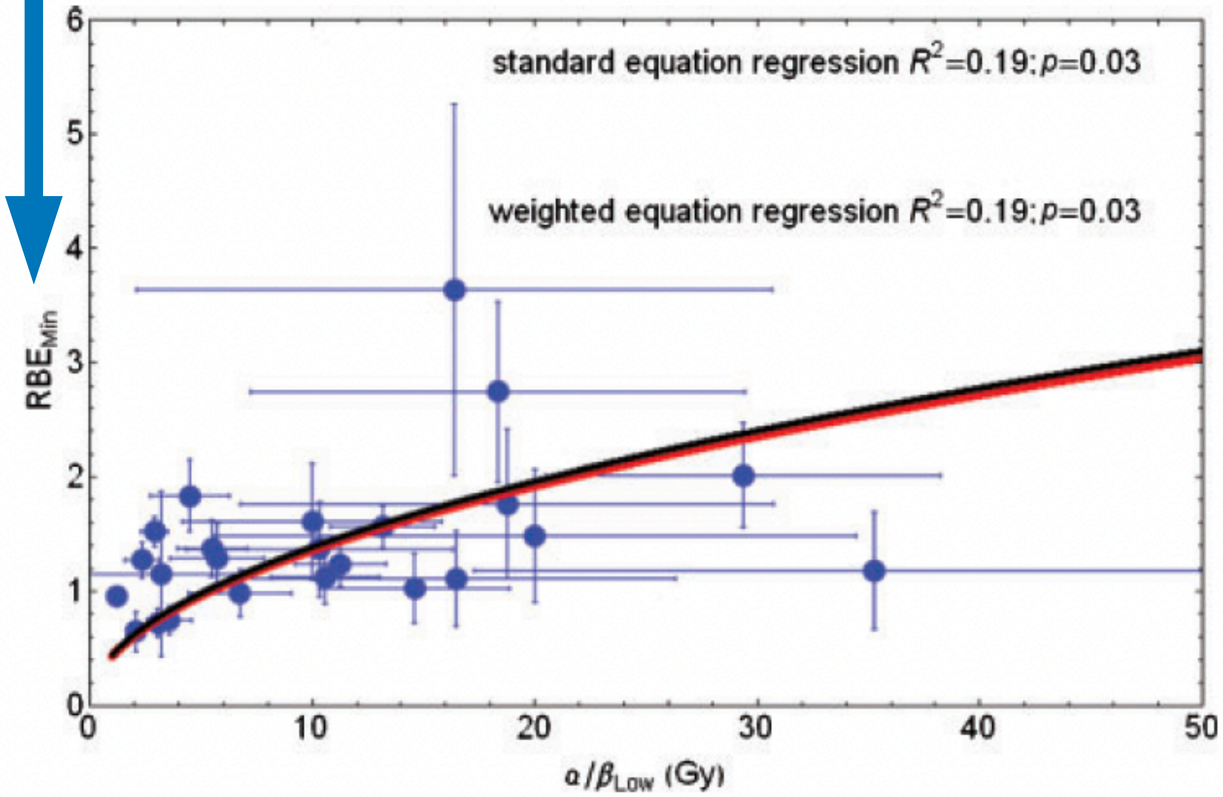
[1,2]B JONES, MSc, MD, [1,2]T S A UNDERWOOD, MPhys, MSc, [3]A CARABE-FERNANDEZ, MSc, PhD, [2]C TIMLIN, MPhys, PhD and [2,4]R G DALE, PhD, FInstP

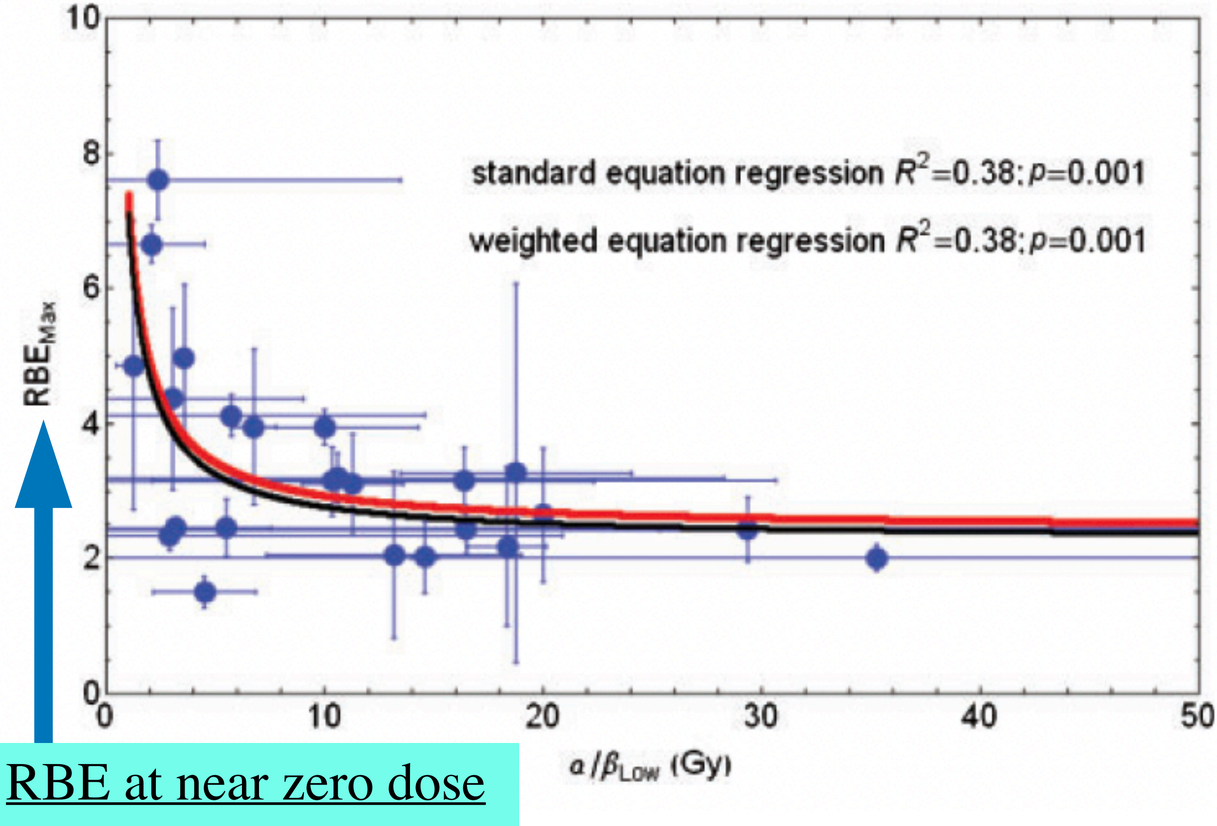
RBE at very high dose

Table 1. Data (point estimates) taken from Carabe-Fernandez et al [4] and used in this report

Assay	Low LET α/β	RBE_{max}	RBE_{min}
Oesophagus, LD_{50}	16.24	3.05	2.27
Bone marrow (haematocrit)	1.15	26.33	1.19
Kidney (EDTA)	1.22	20.58	1.35
Kidney	2.23	15.85	0.73
Mouse skin	17.42	5.35	0.41
Colorectal, LD_{50} (2 months)	28.96	5.70	1.46
Colorectal, LD_{50} (15 months)	3.11	12.56	0.41
Lung (28 weeks)	2.93	7.63	0.58
Lung LD_{50} (28 weeks)	5.95	5.19	0.99
Lung LD_{50} (68 weeks)	2.32	8.62	0.72
Pig skin (acute)	15.17	3.46	0.71
Pig skin (late)	5.25	4.26	0.91

EDTA, ethylenediaminetetraacetic acid; LD_{50}, lethal dose for 50%; LET, linear energy transfer; RBE_{max}, maximum value of relative biological effect; RBE_{min}, minimum value of relative biological effect.





RBE at near zero dose

The British Journal of Radiology, 84 (2011), S11–S18

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RBE at very high dose

extremely large uncertainties

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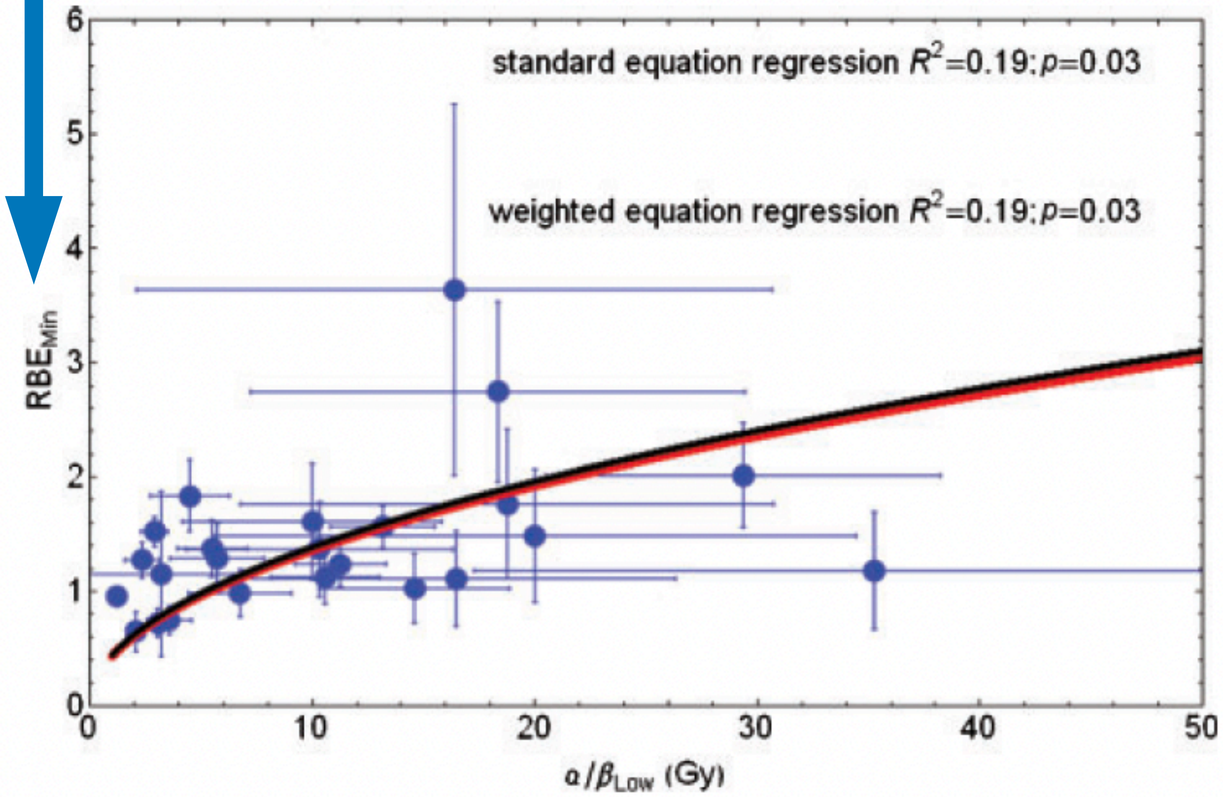
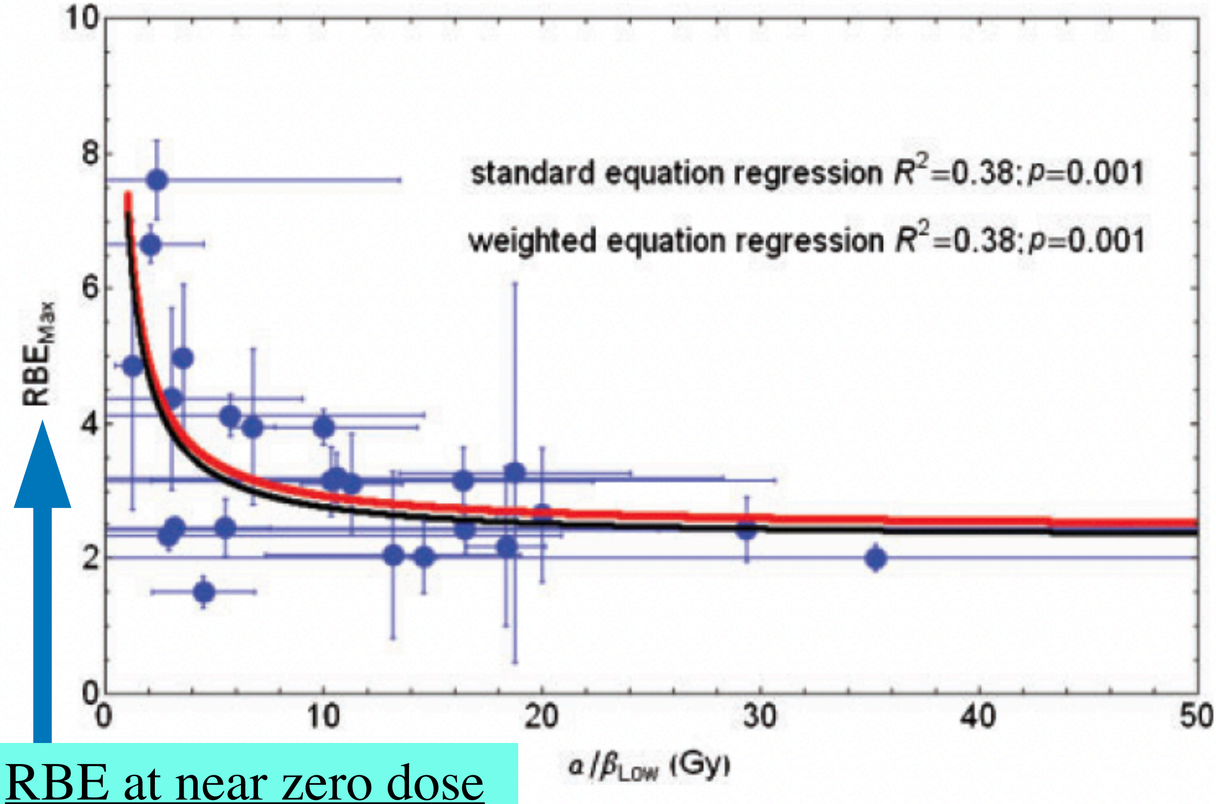
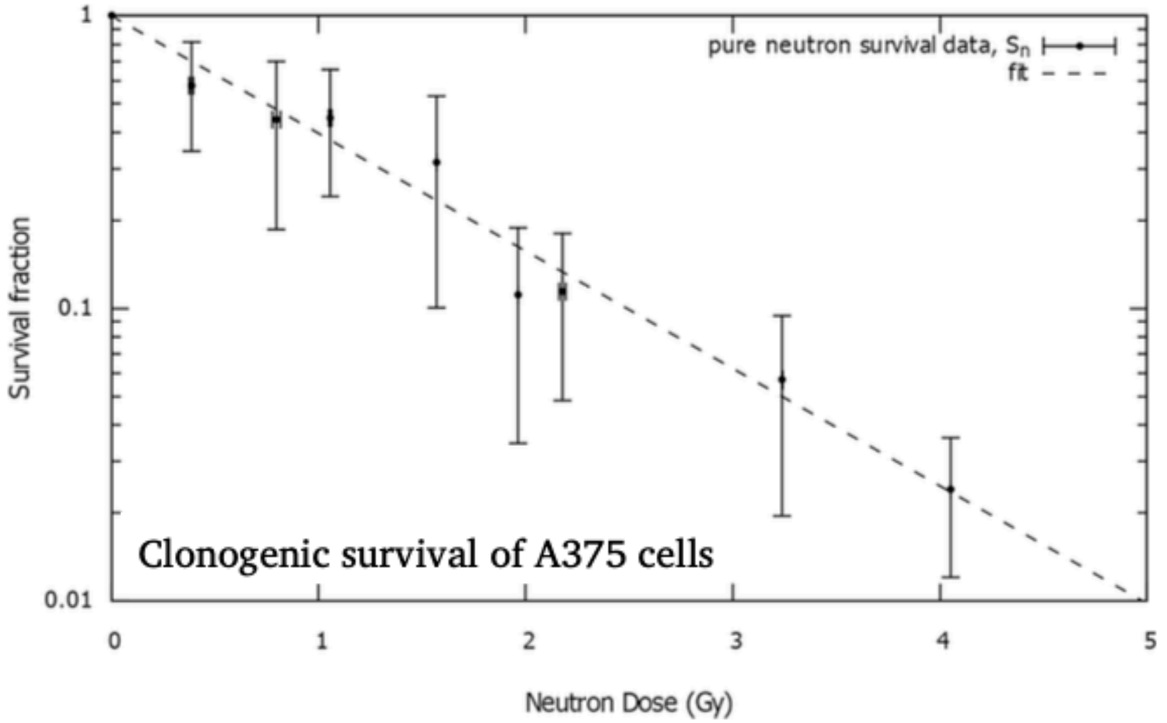




RBE at near zero dose

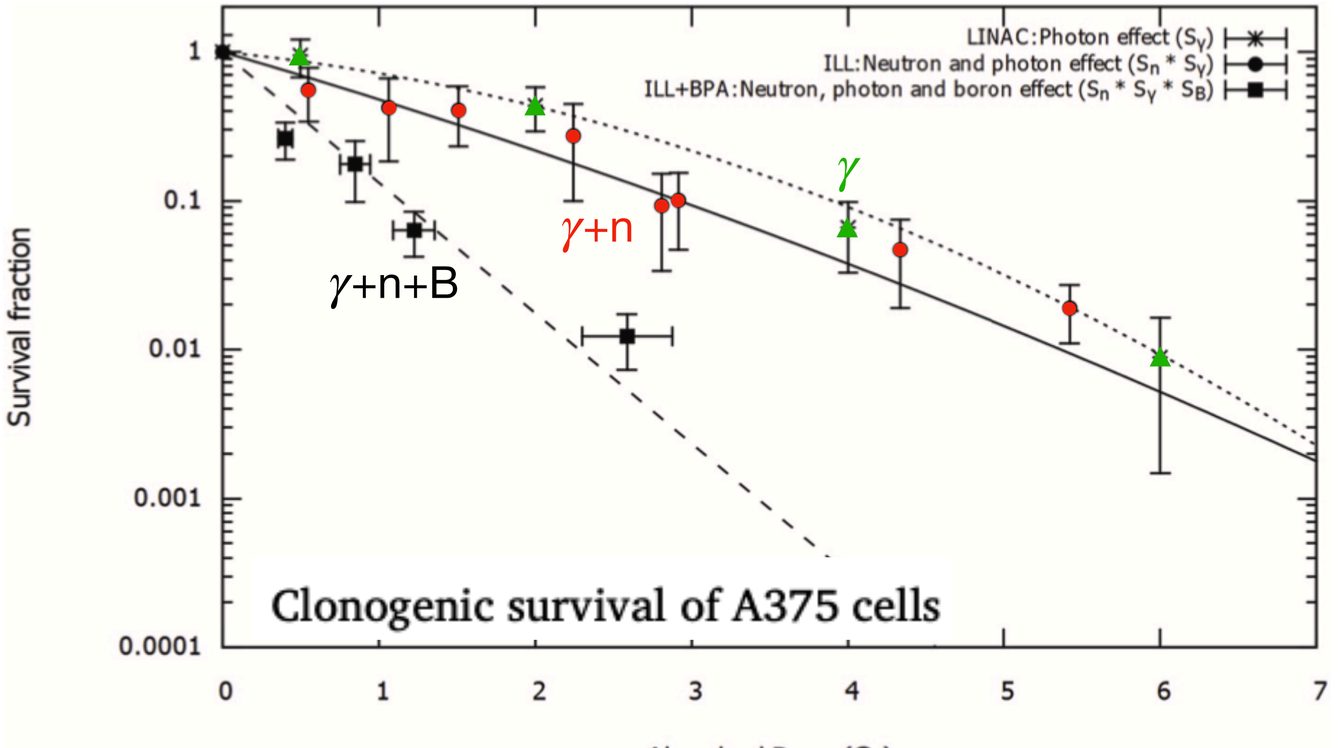
Nuclear Inst. and Methods in Physics Research B 462 (2020) 24–31

Pedrosa-Rivera. et al.



Applied Radiation and Isotopes 163 (2020) 109205

Pedrosa-Rivera et al.



Neutron radiobiology: where we are

A.M. Lallena[1,4], D. Guirado[2,3,4], M. Villalobos[3,4]

[1] Dpto. Física Atómica, Molecular y Nuclear, Universidad de Granada
[2] Unidad de Radiofísica, Hosp. Univ. Clínico San Cecilio, Granada
[3] Dpto. de Radiología y Medicina Física, Universidad de Granada
[4] Instituto de Investigación Biosanitaria (ibs.GRANADA)

Neutron radiobiology: where we are?

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IFMIF-DONES

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- **neutron (and deuteron) beams available will open the possibility of analyzing situations never investigated before**
- **thus complementing the radiobiological information that can be obtained by using the nearby electron clinical accelerators and X-ray irradiation facilities**

IFMIF-DONES would provide an invaluable opportunity to expand our knowledge about the cell response to both neutrons and deuterons

a last message

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From my point of view, and as I have learned preparing this meeting, people from radiobiology, medicine, biology, chemistry, … know almost nothing about IFMIF-DONES and are, probably for this reason, very reluctant to participate and contribute their knowledge

It is necessary to make known the opportunities that IFMIF-DONES can offer to these other communities that are, a priori, far from the project

Santa Catalina Castle
Jaén

Thanks for your attention

La Alhambra
Granada